

PROGRESSIVE MEDICINE





Presented to
The Library
of the
University of Toronto
by

Academy of Medicine

CONTRIBUTORS TO VOLUME IV

1916

J. HAROLD AUSTIN, M.D.
JOSEPH C. BLOODGOOD, M.D.
CHARLES W. BONNEY, M.D.
EDWARD H. GOODMAN, M.D.
H. R. M. LANDIS, M.D.

PUBLISHED QUARTERLY

BY

LEA & FEBIGER

706-710 Sansom Street

PHILADELPHIA

Med
P

Awarded Grand Prize, Paris Exposition, 1900

PROGRESSIVE MEDICINE

A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES
AND IMPROVEMENTS

IN THE
MEDICAL AND SURGICAL SCIENCES

EDITED BY

HOBART AMORY HARE, M.D.

PROFESSOR OF THERAPEUTICS, MATERIA MEDICA, AND DIAGNOSIS IN THE JEFFERSON MEDICAL COLLEGE,
PHILADELPHIA; PHYSICIAN TO THE JEFFERSON MEDICAL COLLEGE HOSPITAL; ONE TIME CLINICAL
PROFESSOR OF DISEASES OF CHILDREN IN THE UNIVERSITY OF PENNSYLVANIA;
MEMBER OF THE ASSOCIATION OF AMERICAN PHYSICIANS, ETC.

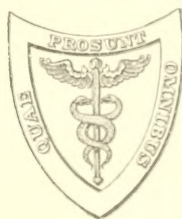
ASSISTED BY

LEIGHTON F. APPLEMAN, M.D.

INSTRUCTOR IN THERAPEUTICS, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA; OPHTHALMOLOGIST TO THE
FREDERICK DOUGLASS MEMORIAL HOSPITAL AND TO THE BURD SCHOOL; INSTRUCTOR IN OPHTHAL-
MOLOGY, PHILADELPHIA POLYCLINIC HOSPITAL AND COLLEGE FOR GRADUATES IN MEDICINE

VOLUME IV. DECEMBER, 1916

DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS, THE LIVER, PANCREAS,
AND PERITONEUM—DISEASES OF THE KIDNEYS—GENITO-URINARY DISEASES
—SURGERY OF THE EXTREMITIES, SHOCK, ANESTHESIA, INFECTIONS,
FRACTURES AND DISLOCATIONS, AND TUMORS—PRACTICAL
THERAPEUTIC REFERENDUM.



24772
22.10.30

LEA & FEBIGER
PHILADELPHIA AND NEW YORK
1916

Entered according to the Act of Congress, in the year 1916, by
LEA & FEBIGER,
in the Office of the Librarian of Congress. All rights reserved.

LIST OF CONTRIBUTORS

J. HAROLD AUSTIN, M.D.,

Associate in Medicine, University of Pennsylvania; Assistant Physician to the University Hospital, Philadelphia.

JOSEPH C. BLOODGOOD, M.D.,

Associate Professor of Surgery, Johns Hopkins University, Baltimore, Md.

CHARLES W. BONNEY, M.D.,

Assistant Demonstrator of Anatomy in the Jefferson Medical College, Philadelphia.

JOHN G. CLARK, M.D.,

Professor of Gynecology in the University of Pennsylvania, Philadelphia.

WILLIAM B. COLEY, M.D.,

Professor of Clinical Surgery, Cornell University Medical School; Attending Surgeon to the General Memorial Hospital for the Treatment of Cancer and Allied Diseases; Attending Surgeon to the Hospital for Ruptured and Crippled, New York.

FLOYD M. CRANDALL, M.D.,

Consulting Physician to the Infants' and Children's Hospital; Late Visiting Physician to Minturn Hospital, New York.

EDWARD P. DAVIS, M.D.,

Professor of Obstetrics in the Jefferson Medical College of Philadelphia.

WILLIAM EWART, M.D., F.R.C.P.,

Consulting Physician to St. George's Hospital and to the Belgrave Hospital for Children, London.

CHARLES H. FRAZIER, M.D.,

Professor of Clinical Surgery in the University of Pennsylvania; Surgeon to the University, Howard, and Philadelphia Hospitals.

JOHN C. A. GERSTER, M.D.,

Instructor in Operative Surgery, Cornell University; Adjunct Surgeon, Mount Sinai Hospital; Assistant Surgeon, Knickerbocker Hospital, New York.

EDWARD H. GOODMAN, M.D.,

Associate in Medicine, University of Pennsylvania; Assistant Physician, University Hospital and Philadelphia General Hospital; Consultant to the Medical Dispensary, University Hospital, Philadelphia.

WILLIAM S. GOTTHEIL, M.D.,

Adjunct Professor of Dermatology, New York Post-Graduate Medical School;
Consulting Dermatologist to Beth Israel and Washington Heights Hospitals;
Visiting Dermatologist to the City and Lebanon Hospitals, New York City.

EDWARD JACKSON, M.D.,

Professor of Ophthalmology in the University of Colorado; Ophthalmologist
to the City and County Hospital of Denver.

H. R. M. LANDIS, M.D.,

Director of the Clinical and Sociological Departments of the Henry Phipps
Institute of the University of Pennsylvania; Assistant Professor of
Medicine in the University of Pennsylvania; Visiting Physician to the
White Haven Sanatorium.

GEORGE P. MÜLLER, M.D.,

Associate in Surgery in the University of Pennsylvania; Professor of Surgery
in the Philadelphia Polyclinic and College for Graduates in Medicine; Sur-
geon to the St. Agnes and Polyclinic Hospitals; Assistant Surgeon to the
Hospital of the University of Pennsylvania; Consulting Surgeon to the
Chester County Hospital.

JOHN RUHRÄH, M.D.,

Professor of Diseases of Children and Therapeutics, College of Physicians
and Surgeons; Visiting Physician, Robert Garrett Hospital, Nursery and
Child's Hospital, Mercy Hospital; Consulting Physician, Church Home and
Infirmary, Baltimore.

TRUMAN LAURANCE SAUNDERS, A.B., M.D.,

Chief of Clinic, Vanderbilt Clinic, and Instructor in Otology in the College of
Physicians and Surgeons (Columbia University); Chief Assistant Surgeon
of the New York Eye and Ear Infirmary; Assistant Surgeon of the Man-
hattan Ear, Nose, and Throat Hospital; Attendant Otologist of the Minturn
Hospital, New York.

WILLIAM G. SPILLER, M.D.,

Professor of Neurology in the University of Pennsylvania; Clinical Professor
of Nervous Diseases in the Woman's Medical College of Pennsylvania.

ALFRED STENGEL, M.D.,

Professor of the Theory and Practice of Medicine and Clinical Medicine in
the University of Pennsylvania, Philadelphia.

GEORGE B. WOOD, M.D.,

Surgeon to the Department of the Nose, Throat, and Ear, Howard Hospital;
Laryngologist, Orthopædic Hospital.

CONTENTS OF VOLUME IV

DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS	
THE LIVER, PANCREAS, AND PERITONEUM	17
BY EDWARD H. GOODMAN, M.D.	
DISEASES OF THE KIDNEYS	137
BY J. HAROLD AUSTIN, M.D.	
GENITO-URINARY DISEASES	179
BY CHARLES W. BONNEY, M.D.	
SURGERY OF THE EXTREMITIES, SHOCK, ANESTHESIA, INFECTIONS, FRACTURES AND DISLOCATIONS, AND TUMORS	229
BY JOSEPH C. BLOODGOOD, M.D.	
PRACTICAL THERAPEUTIC REFERENDUM	369
BY H. R. M. LANDIS, M.D.	
INDEX	

PROGRESSIVE MEDICINE.

DECEMBER, 1916.

DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS, THE LIVER, PANCREAS, AND PERITONEUM.

By EDWARD H. GOODMAN, M.D.

DISEASES OF THE MOUTH AND ESOPHAGUS.

THIS year has provided more difficulties in securing foreign publications even than last year. Then it was possible to receive foreign journals even though belated, but this year certain periodicals seem impossible to obtain. The reviewer has been accustomed to receive the most important German journals, and from these he has made his abstracts. Unfortunately, such publications are now sent only at the subscriber's risk, and but few will assume this. Fortunately, on the other hand, the *Journal of the American Medical Association* receives fairly regularly the journals which it has been in the past our pleasure to read, and the editorial staff has, happily, reviewed the most important articles. We have made free use, therefore, of the *Journal's* abstracts, and we acknowledge with much appreciation and esteem most highly the very comprehensive reviews which appear in the *Journal*. Apologies for abstracting an abstract under ordinary conditions should be made if the deed itself can be condoned, but apologies, at present, are hardly necessary since the explanation of why we have made use of the vicious practice should dull the edge of reproach.

Mouth. SALIVA. The *viscosity of saliva* depends upon the quality of food. Lubimoff¹ found that the saliva of dogs becomes less viscous if they are given dry toast at five-minute intervals. If then the saliva is passed through a narrow glass tube, it will be found that the first portion requires fifteen seconds for its passage, the third fourteen seconds, the last portion twelve seconds. When given 10 c.c. of hydrochloric

¹ Abstract Journal of American Medical Association, 1915, lxy, 987.

acid (0.25 per cent. solution) every five minutes, collecting each time the saliva in test-tubes. Lubimoff found that the viscosity of the saliva increased and the secretion was more profuse. These and other tests showed that repeated frequent irritation of the salivary glands with food causes not only a diminution in the quantity of saliva but also in its content of solid substances. Substances other than food have just the opposite results.

Hatta¹ tabulates his findings in the saliva in respect to *quantity, ferment content, and variations in response to different stimuli*. The salivary diastase content did not seem to be directly influenced by the kind of food, and it showed no characteristic fluctuations in any of the diseases investigated. Tannic acid, even in minute amounts, inhibited the diastatic power of the saliva, while sodium nucleinate magnified it tenfold when in a concentration of 1.5 per cent. Below this, no effect was evident, and above 3 per cent. it actually caused inhibition. Tincture and extract of valerian promoted ferment action, this effect being most pronounced at a concentration of 7 per cent. Aqueous extracts may have a more favorable action than the tinctures, especially those of strophanthus, strychnine, and ipecac. The enzyme content secreted during chewing is higher than of saliva spontaneously flowing into the mouth. Still higher diastatic power was found in saliva secreted under the influence of citric acid. Hatta calls attention to the remarkably constant proportion between the amount of saliva secreted and the ferment content, no differences at any time being found between the amount of saliva and the ferment power, no differences at any time being found in this proportion in specimens of saliva obtained in health, from the same person at the same time of day and under the same stimuli. The diastatic power kept unmodified for six months in saliva preserved under a layer of toluol, but it was lost in a month in saliva preserved merely by a layer of formaldehyde or phenol. Six of the sugars had no influence below a concentration of 1.5 per cent.; above this they seemed to depress the diastatic content.

Solem and Lommen² have made some observations on the *effect of the posterior lobe of the hypophysis upon the secretion of saliva*. It has been contended that pituitary extract has no influence on the chorda tympany nerve or on the secretory nerves of the salivary gland, but the authors above named have reopened this question and have attempted to determine whether the effect is due to vascular changes in the organ or to a specific action on the cells or on the secretory nerves. Their work has shown that pituitrin invariably caused a diminution in the flow of blood and saliva, but that the decrease in the latter was greater than the accompanying decrease in blood flow. This decrease, they conclude,

¹ Abstract Journal of American Medical Association, 1916, lxvi, 930.

² American Journal of Physiology, 1915, xxxviii, 338.

must be due to inhibition of the secretory nerve to the salivary gland, but vasoconstriction also plays a role, this being brought about by action on the muscles of the arterioles and on the peripheral endings of the vasomotor nerves.

RELATION OF SALIVA TO PEPTIC DIGESTION. FUNCTION AND PURPOSE OF PTYALIN. Maxwell¹ regards it as a curious fact that an enzyme (ptyalin) should be secreted in the mouth to be presently destroyed in the stomach, while a more efficient diastase is present in the secretion of the pancreas. Perhaps an important function of ptyalin is to act as a stimulant to the formation of gastric secretion by the production of dextrin from starch hydrolysis. Reasoning that charcoal and certain powders have the power of absorbing enzymes, he theorized that colloidal starch solutions may act the same way, *i. e.*, may absorb pepsin by the colloidal carbohydrate and would thus aid gastric digestion.

Maxwell allowed pepsin to act on fibrin in the presence of either colloidal starch solutions or starchy foods and compared the rate of digestion with that which occurred after previous hydrolysis of the carbohydrate by saliva or taka diastase. He found, as he had supposed, that peptic digestion is delayed in the presence of colloidal starch solution through absorption of enzyme, the time interval being increased fourfold in the presence of 2 per cent. starch solution. There is a stage in the disruption of the starch molecule at which this phenomenon of absorption of pepsin is lost. This occurs between the amylopectin and erythropectin stage. An interesting point brought out in his experiments is that unboiled starch does not hinder peptic action, a factor of importance in the dietetics of herbivora; cooked farinaceous foods—rice, potato, bread—all hinder the action of pepsin if not first subjected to salivary digestion. Maxwell concludes, therefore, that the saliva of man, by virtue of its ptyalin, plays a considerable part in aiding gastric digestion by hydrolyzing colloidal starch, which would otherwise absorb pepsin.

Nervous Furring of the Tongue. "There is no more ineradicable idea in the mind of the doctor than that the furred tongue is essentially an indication of a deranged stomach, and it is probably an attempt to kick against the pricks to say otherwise. That a dirty tongue is an indication that the liver is out of order and that a purge of some sort is the one and only remedy, will, I suppose, never cease to be thought as long as the world lasts, and in a fair proportion of cases I am not prepared to traverse the practice. But it is by no means always so, a dirty tongue does not mean a foul stomach, and there is always scope in the vision for interesting thought and inquiry."

Goodhart,² who penned the above, is a believer in the doctrine which holds that a furred tongue is as often caused by the head as by the stomach; in other words, there are certain taut and tense individuals.

¹ Biochemical Journal, 1915, ix, 323.

² Lancet, 1915, ii, 691.

as well as the hypochondriacs and slackers, who present dirty tongues as an accompaniment of their temperaments. Cases are quoted to exemplify this teaching. Goodhart recalls the rapid appearance of fur on the tongue and the sudden development of fetid breath in cases of fracture of the base of the skull, and in hemiplegia. Obviously, this may be due to various causes: To liquid food hanging about the mouth and then decomposing, lack of care of the teeth, failure of the movement of the tongue and palate to assist in removing foreign elements; but allowing for all this, he believes it is the loss of nervous control over the material processes that in health tend to keep the mouth sweet and wholesome which is the *fons et origo* of the furred tongue and perverted taste.

The author is a firm believer in the neurasthenic taint, and applies his faith in other directions—the gastro-intestinal tract—where modern surgery would be robbed of half its brilliancy could a continuous flow of nervous energy be substituted for the poor and miserably intermitting one. He says he has read that “Quinney squirmed at the remote possibility of being merged and lost. He muttered uneasily, ‘It fair furs my tongue to think o’ that.’”

Whether explaining to the afflicted the rationale of his disorder will satisfy him is doubtful, for Goodhart observes that it is a sad but true piece of human experience that many a sick man feels himself safe when *vis a vis* with his doctor, who later becomes prone to dwell upon his loneliness if he be unaccompanied by the customary bottle of physic.

Esophagus. **CARDIOSPASM.** A very able paper by Held and Gross¹ brings the subject of cardiospasm up to date in a comprehensive manner. By cardiospasm they understand a spastic contraction of the cardia of longer or shorter duration, leading to hypertrophy and to dilatation above the contraction. Spasms elsewhere in the esophagus are called esophagospasm, and occur at one of the physiological narrowings of the esophagus, at the cricoid cartilage, at the bifurcation of the trachea, and at the entrance of the opening of the diaphragm.

The authors review the physiology of the act of deglutition, the main points of which review seem to be, for our consideration here, the fact that the propulsion time of material through the esophagus is dependent on whether fluids, solids, or semisolids are swallowed. The upper part of the esophagus propels the food rapidly without peristalsis, while the lower part, where striated muscle is seen, propels it slower and with peristaltic movements. Another important feature in Held and Gross's review is that the act of deglutition is a reflex one, the center being in the medulla oblongata.

The nervous control of deglutition is next considered, but of particular interest is the innervation of the lower esophagus and cardia. The motor function is derived from the vagus, but there are sympathetic nerve

¹Journal of the American Medical Association, 1916, lxvi, 233.

fibers on the lower esophagus also. Indeed, if the vagus function be impaired, the intrinsic nerves of the lower esophagus and cardia are well able to carry on the function. Functional disease of the vagus as well as organic disease may bring about disturbances in deglutition. Held and Gross devote considerable space to vagotonia and to sympathetico-tonia which is unfitted for review here.

Generally speaking, cardiospasm is believed to be due to vagus irritation, and the underlying factors bringing about such a state are divided into five groups.

First Group. Vegetative nervous system below par through inheritance. Even in childhood a history pointing to vagotonia or sympathetico-tonia will be found (enuresis nocturna, periodic vomiting, laryngospasm).

Second Group. Involvement of vegetative nervous system through status lymphaticus or thymicolymphatics. Such individuals cannot assume great responsibilities, either physical or mental, and when overtaxed, rapidly show functional derangement in the vegetative nervous system. In this group, Held and Gross place cases of gastrotonia, especially "long stomach," in which traction on the esophagus is said to be the causative factor. Cardiospasm also belongs in this group.

Third Group comprises individuals who show cardiospasm secondary to irritation from diseased organs (gastric ulcer, gastric carcinoma, gallstones, renal calculi, genito-urinary diseases, chronic pancreatitis, left-sided diaphragmatic pleurisy).

Fourth Group. Cases of cardiospasm due to toxic or metabolic agents.

Fifth Group. Cases in which a local esophageal disease is the causative factor (fissure, erosions, scar-tissue formation, peptic ulcer of the gullet). The disease is generally found in young individuals, and in men as frequently as in women.

Symptomatology. Characteristically, deglutition is suddenly, and may be only transiently, affected. In other instances the attack may last for weeks or months. Patients will state that solids pass, while fluids are obstructed. If the spasm is persistent, food stagnation takes place—belching, regurgitation and pain. Pain may, or may not, be present; it is out of all proportion to the degree of the disease—cold water may cause violent distress. If there is a fissure accompanying spasm, deglutition pain is a prominent symptom.

Objective examination is important, but, of all the methods, Röntgenoscopy stands pre-eminent.

Treatment is to be that of the etiological factor. In cases of vagotonia, hydrotherapeutic measures, change of climate, physical and mental rest, together with psychotherapy, are all indicated. As far as diet is concerned, the food should include cream, butter, cereals, cream soups, spinach, carrots, peas, cauliflower, soft-boiled eggs. Meat should be scraped or

or minced, and toast or zwieback should be allowed to dissolve in the mouth before swallowing. Food should be neither too hot nor too cold when eaten.

Atropine is very useful, and hypodermic injections of from 0.0005 to 0.001 gm. once or three times a day are valuable. When improvement is finally seen, 0.5 mg. of atropine should be given every second day for at least a month. When hypodermic medication cannot be carried out, extract of belladonna, 0.015 to 0.03 gm., in the form of suppositories, are to be used.

Instrumental treatment is indicated only when medical measures fail.

VALUE OF X-RAY IN DIAGNOSING ESOPHAGEAL CONDITIONS. Elsner and Ury¹ emphasize the fact that they have in this work approached diseases of the esophagus from the clinical as well as from the röntgenologic aspect, and think, in so doing, they have arrived at more accurate conclusions than are usually attained when the subject is studied from the *x*-ray side alone. The value of the *x*-ray examination is recognized, particularly when carcinoma is present, but it is stated by the authors that in 96 per cent. of the cases the condition was correctly diagnosed from the history and after sounding, and the *x*-ray but clinched the diagnosis. There are certain cases, however, when the diagnosis cannot be made accurately, and in these instances the *x*-ray is of untold value. Esophageal sounds may entirely fail to reveal any obstruction, but the *x*-ray rarely fails to show some slight delay in the passage of bismuth along the gullet, but even when slight, one should think of the possibility of esophageal cancer.

The above holds even more true for carcinoma of the cardiac end of the stomach, for here the diagnosis is much more difficult. Whereas, doubtful cases of esophageal neoplasms are rare, owing to the almost constant presence of difficult deglutition and obstruction to the passage of food, in carcinoma of the cardia, however, there may be no difficulty in swallowing and no obstruction to the passage of the esophageal sound. The *x*-ray here is of prime importance, for it reveals the bismuth remaining for a longer or shorter period of time just above the cardia. When the time of stagnation is long, the lower portion of the esophagus assumes a sausage- or funnel-shape, and the whole esophagus seems to be considerably dilated.

Of less importance to the authors' minds is the use of the *x*-ray in diagnosing benign conditions of the esophagus, particularly of spasm. In these instances physical examination generally proves to be entirely negative, but the *x*-ray may show a transient damming back of the bismuth emulsion, then a sudden propulsion forward, coincident with cessation of all subjective symptoms.

Chronic cardiospasm, with secondary ectasia of the esophagus, is

¹ Arch. f. Verdauungskr., 1915, xxi, 289.

more frequent and the esophagus may be greatly widened. There are many cases in which three-quarters of a liter may be poured into the dilated tube. But in these instances the diagnosis can be made without the use of the *x*-ray, when the following symptoms and findings are considered: Regurgitation and vomiting of food, some of which may have been eaten a long time previously, the presence of decomposed food-rests in the esophagus of the fasting subject, lactic acid in this mass of food, and the inability to pass a sound through the cardia. Although the diagnosis itself may seem simple enough, it is very important that one should appreciate the shape and the degree of esophageal dilatation, both of which it is impossible to recognize without the assistance of the röntgenologist.

Elsner and Ury conclude their article, which is not confined to the discussion of the esophagus, but which comprises the consideration of the value of the *x*-ray in gastric conditions, by saying that the Röntgen ray has no value in the diagnosis of carcinoma, as the condition can be readily recognized from the history and examination. For the diagnosis of cardiac carcinoma it is most useful, for at times sounding fails to reveal any obstruction. In cardiospasm with secondary cetasia, the *x*-ray supplements the clinical diagnosis, but does more than this, as it furnishes us in plastic form an impression of the shape and size of the esophagus.

DISEASES OF THE STOMACH.

Gastric and Duodenal Ulcers. The questions, Are there any symptoms or a group of symptoms whereby we may reasonably locate peptic ulcer? Do clinically histories, as ordinarily taken, give satisfactory evidence as to whether the ulcer be high or low? are answered by Graham¹ in the negative. He calls attention to three clinical syndromes which he believes should be considered:

1. *The Regular Type of Duodenal Ulcer* is expressed clinically by pain or distress coming on within two to five hours after meals, accompanied by gas, sour stomach and vomiting, all these continuing until the next meal, or until relieved by alkali, vomiting, or gastric lavage. These symptoms repeat themselves for a shorter or longer period of time, then a marked remission occurs, the periods of attack and intermission continuing for years.

2. *The Regular Gastric Type* resembles the duodenal type in symptoms and in periodicity, though the former are not so clear cut. Pain or distress occurs earlier after eating, it is not of so long duration, it may be eased by the taking of food. Fear of food-pain is more often noted.

* ¹ Boston Medical and Surgical Journal, 1917, clxxii, 543.

while hunger-pain is not so pronounced. Careful dieting is followed by more relief than is the case with duodenal ulcer. The position of the body and physical activity play a more important role in the gastric than in the duodenal cases.

3. *The Irregular Peptic Ulcer Type.* Here there are missing the distinctive time of onset of symptoms and their control. Intermissions or remissions are fairly constant, but not so well defined. The history does not give the daily distinctive time of onset and control of symptom. Although there is this irregular course, yet, when the case is surveyed after days and weeks, we find in the irregularity a more or less definiteness which indicates a gastric lesion. Hunger pains, food ease and hemorrhage are not constant, but pain, vomiting, distress, gas and sour eructations are the constant results of food intake, from which relief is procured by careful diet, irrigation, alkalies or lavage.

Histories in cases of high ulcer are of this third type, those of pyloric and duodenal ulcer less frequently, thus a diagnosis of gastric rather than of duodenal ulcer is preferable in the presence of such a history, or we look for extrinsic causes. Duodenal histories from 1906 to 1915 have demonstrated to Graham that 72 per cent. of duodenal cases gave fairly regular histories, and 71 per cent. of gastric cases were almost typically gastric. In all peptic ulcers, pain is present in more than 99 per cent. It is described as distress, aching, burning, gnawing, pressing, boring, sharp cramps, colic, etc. In the duodenal cases, pain came after food in 23 per cent., and two to five hours in 77 per cent. of the cases. In gastric ulcers, the time limits of a half to two hours included 50 per cent. and two to five hours, 50 per cent. Night pain is more constant in duodenal ulcers. In 49 per cent. of the duodenal ulcer cases pain was confined to the epigastrium, while 52 per cent. of the gastric were similarly located. Those with radiation to the back ran 24 per cent. duodenal and 22 per cent. gastric. Radiation to the left epigastric area occurred in 10 per cent. of gastric ulcer and in 4 per cent. of duodenal ulcer. Radiation to the abdomen and fossæ occurred in 9 per cent. in both cases. Radiation to the right epigastrium was present in 6.6 per cent. of the gastric cases and in 13.7 per cent. of the duodenal. It will be noted, therefore, that tenderness to touch and radiation of pain are of little value in differentiating gastric from duodenal ulcer.

Vomiting occurred in 79 per cent. of the duodenal, and in 82 per cent. of the gastric ulcers, while gas was present in 77 per cent. of the duodenal and in 94 per cent. of the gastric cases. Gastric hemorrhages were recorded in 18.5 per cent. of the duodenal and in 25 per cent. of the gastric cases, and blood in the stools was found in 18 per cent. (duodenal) and in 24 per cent. (gastric). See table on opposite page for comparison of clinical diagnoses in cases of operatively demonstrated duodenal and gastric ulcers.

Graham concludes this admirable summary by saying: "Each case necessarily calls for its own careful consideration, because no symptom, or group of symptoms, can more than suggest location, and often, as our histories show, the gastric case may have the pure duodenal syndrome and the duodenal case may quite as clearly give the gastric type of symptoms. The diagnosis of a gastric lesion made, the question of its exact location is not paramount. How best to treat the lesion and conserve the patient's health is the vital point."

Clinical diagnosis	1300 duodenal ulcers		43 gastric ulcers	
	Cases	Per cent.	Cases	Per cent.
Primary diagnosis, duodenal ulcer	702	54.0	248	55.0
Primary diagnosis, gastric ulcer	323	24.8	110	26.5
Secondary diagnosis, duodenal or gastric ulcer (repeated)	107	8.2	31	6.5
Primary diagnosis: diseased gall-bladder (gall-bladder alone 5 per cent.)	175	13.5	40	8.8
Primary diagnosis: appendicitis (appendicitis alone 1+ per cent.)	64	5.0	8	1.7
Primary diagnosis: cancer		1.5	22	4.8
Unclassified		1.0		2.8
Time and appearance of pain:				
One-half to two hours (per cent.)		23.0		50.0
Two to five hours (per cent.)		77.0		50.0
One-half to one hour (per cent.)		8.0		10.0
Pain at night		14.0		10.0
Postural case		8.0		9.0
Location or radiation of pain:				
Epigastrium		49.0		52.0
Radiation to back		24.0+		22.0+
Radiation to left epigastrium		4.0		10.0+
Radiation to abdomen and fosse		9.5		9.0+
Radiation to right epigastrium		13.7		6.6
Control of pain:				
Food or drink or both		75.0		66.0
Alkalies		38.0		33.0
Irrigation		11.0		9.0
Diet		20.0		22.0
Pain continuous from onset of symptoms		4.0		9.5
Tendencies to touch		41.0		48.0
Vomiting		79.0		82.0
Gas		77.0		94.0
Hemorrhage by mouth		18.5		25.0
Blood by bowel		18.5		24.0
Perforation		28.7		26.0
Perforation into pancreas		17.0		25.0
Obstruction		26.0		10.0

FIG. 1

DIVERTICULUM OF THE STOMACH FOLLOWING GASTRIC ULCER.¹ Long before the röntgenologic era it was recognized that certain anatomical changes in the stomach would be productive of diverticula. Since the *x*-ray examination has been universally employed, it was found for the first time by Haudek that certain "Nischenbildungen" (niche formations) and even true diverticula were not a rare accompaniment of perforating gastric ulcers. Strauss recognizes that such pathological conditions do exist, but believes they occur extremely rarely, while de Quervain, in a relatively meagre operative material, has encountered it twenty times. In these twenty cases, at operation there was found a projection or diverticulum of the stomach, extending either into the ligamentum hepatogastricum, or into the adherent liver or pancreas. The operative

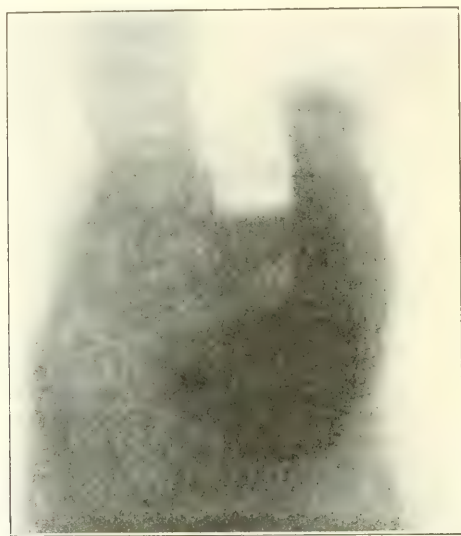


FIG. 2.—Diverticulum with "luft blase." Standing.

findings corresponded exactly with the *x*-ray reports. de Quervain disagrees with Strauss as to the infrequency of such niches, and believes that not rarely does a penetrating ulcer of the lesser curvature give rise to diverticulum formation.

In certain cases the ulceration, particularly in the region of the gastrohepatic ligament, eats into this ligament, giving rise to only a depression in the *x*-ray picture and at operation. Whether these depressions ultimately give rise to diverticula, must be determined only after years of observation with the *x*-ray, an observation which for very good reasons cannot be made at the present. That such diverticulum

¹ de Quervain, Mitt. a. d. Grenzgeb., 1915, xxviii, 690.

formation can arise, de Quervain believes probable, since in one case he found in a röntgenogram, above the middle of the lesser curvature, a pronounced niche, and another anomaly about 8 cm. lower, which he could not decide from the plate alone, whether it was a beginning niche or but an evidence of contraction. At operation it was found that the uppermost ulcer had produced a true niche, while the lowermost had given rise to only a depression, representing steps in the same process.

In other cases another method of production seems to take place. If an ulcer perforates, depending on the size of the perforation and on the amount of the material in the stomach, there results either an extensive invasion of the peritoneal cavity or merely an area of focal inflammation, which is immediately surrounded by fibrin and which

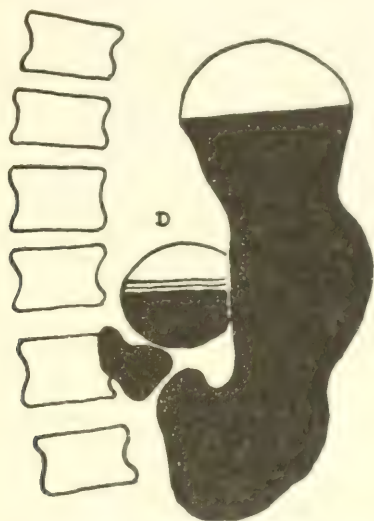


FIG. 3.—Schematic drawing of Fig. 2.

gives rise to a circumscribed perigastric abscess. Sometimes it is only the space between the liver, the anterior wall of the stomach and the ligamentum hepatogastricum which is invaded, in other cases it is the bursa omentalis minor, and even the entire subphrenic space. The abscess cavity finally leads to outgrowth of the stomach wall, in time leading to a niche and finally to diverticulum formation. In the majority of his cases de Quervain finds a history of pain lacking, which inclines him to the belief that such a method of formation must be infrequent. He reminds us, on the other hand, of the rarity of pain in minute perforations.

I reproduce illustrations from de Quervain's article showing true diverticula.

CARBOHYDRATE FACTOR IN THE CAUSATION AND TREATMENT OF HYPERACIDITY AND ULCER. Stone¹ comments on the possible relationship between ulcer and the following:



FIG. 4.—Recumbent.

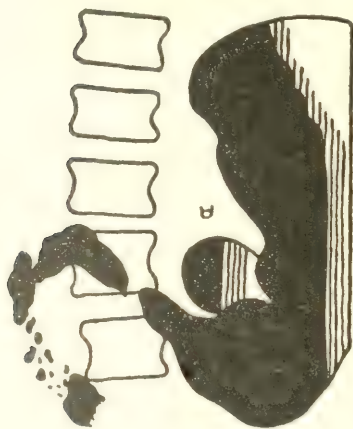


FIG. 5

1. The great increase per capita of sugar consumption during the past fifty years.

¹ Journal of American Medical Association, 1916, lxvi, 324.

2. The possible relationship existing between the increase of sugar consumption and the apparent increased incidence of gastric and duodenal ulcer.



FIG. 6

FIG. 7.—Schematic representation
of Fig. 6.

FIG. 8.—Profile; normal stomach.

3. The influence of restricted carbohydrate diet in the treatment of uncomplicated hyperacidity and ulcer.

The stomach has no provision for the digestion of carbohydrates, and hence a carbohydrate meal is rapidly passed through the stomach for digestion in the intestine. With mixed meals, considerable carbohydrate remains in the stomach during the protein digestion favoring bacterial decomposition, whose products irritate the gastric mucosa and promote hypersecretion.

Believing that there is this strong carbohydrate factor in hyperacidity and in ulcer, Stone treats his patients by allowing no food which contains more than 10 per cent. carbohydrates; fresh fruit pulp and fruit juices (grapefruit, oranges, peaches, and watermelon all without sugar), broth, soft-boiled or poached eggs, fish and chicken, boiled or hashed meats, bacon, milk, tea, cream, butter, green vegetables (asparagus, spinach, cauliflower, watercress, endive, squash, carrots, turnips, lettuce), fruit and lettuce salads with olive oil or lemon-juice dressing, Brazil nuts, pecans, filberts. He prohibits the following: apples, pears, bananas, cherries, currants, plums, peas, parsnips, baked beans, potatoes, green corn, cereals, boiled rice, macaroni, bread, crackers, cocoa, chocolate, and coffee.

If this form of diet does not mitigate the symptoms, a glass of milk is administered between meals and a powder of magnesium oxide and sodium bicarbonate each 20 grains after each feeding. If there is much bacterial decomposition, gastric lavage with salicylic acid, 1 to 1000 once daily before the principal meal may be practised.

GASTRIC ULCER AND HYPERACIDITY DIET. Varipaieff¹ recommends the following diet for hyperacidity and gastric ulcer. At 6:30 A.M. he gives a teaspoonful of bismuth subnitrate with from 3 to 7 drops of belladonna. At 7 A.M. a teaspoonful of calcined magnesia with from 3 to 7 drops of belladonna, and at 7.15 A.M. two raw eggs well beaten. At 9 A.M. (beginning the second day) one teaspoonful of calcined magnesia or calcium carbonate (*calcaria carbonica*) and at 9.15, two eggs. At 11 A.M. (the third day) a teaspoonful of magnesia in calcium carbonate and two eggs. At 1 P.M. is given, per rectum, 30 grams of glucose in 500 c.c. of water; at 4 P.M. this is repeated. At 6 P.M. several doses of oil, altogether about 100–150 grams, after the stomach contents have been rendered alkaline. Thus the patient is getting from 1000 to 1500 calories during the twenty-four hours. The loss of weight with such an insufficient diet is noticeable only during the first two or three days. This dieting was kept up until the pain disappeared, not less than a week. Milk was not allowed until the second or third week, and by this time the oil was stopped. No narcotics were given except the belladonna, and this on account of its specific action on ulcers of the stomach. The

¹ Abstract Journal of American Medical Association, 1915, lxy, 836.

treatment must, of course, be individualized. It was successfully carried out in twelve patients whose histories are given.

EXPERIMENTAL GASTRIC ULCER. WHY GASTRIC MUCOSA DOES NOT DIGEST ITSELF. In *PROGRESSIVE MEDICINE*, 1913, page 27, I wrote under the heading "Etiology of Gastric Ulcer" as follows: "It is of prime importance, in searching for the etiology of gastric ulcer, to comprehend the reason why the stomach under normal conditions does not digest itself. There can be scarcely any doubt but that gastric ulcer is a digestion ulcer, for it arises in the stomach only in those places which are in contact with the active gastric juice. Katzenstein some years ago produced a gastro-enterostomy and then injured the mucous membrane, in two corresponding places, in the stomach and in the intestine. In two days the gastric ulcer was healed, while the intestinal ulcer was in the same condition as before. He concluded that injury was not the only factor in the causation of gastric ulcer, but that, in addition, gastric juice was required. Furthermore, he concluded that the intestinal mucous membrane behaves differently from the gastric mucosa. This is in direct contradiction to Neumann's teaching that all living tissue behaves in the same way toward the digestive juices.

"Katzenstein sought to learn whether there was not an inherent property in living tissue of various kinds whereby they reacted in different ways to the digestive juice. He implanted in the stomach portions of the stomach, duodenum, intestine and spleen without disturbing in the least the mesenteric blood supply, and discovered that the stomach and duodenum were not attacked, while the other structures were digested. From this work he deduced that living tissue in the normal individual can be digested by the stomach, and that the tissues which produce the gastric juice, or are bathed continually in it, are resistant on account of an "Anpassungsvorgang."

"The resistance of the duodenum and stomach to digestion when implanted in the stomach, is held by Katzenstein to be due to the presence of antipepsin. He believes that the stomach and the duodenum pick out the antitrypsin from the circulating blood in the same way that the renal epithelium does with the urinary substances." Based on this theory, Katzenstein reduced the antipepsin in the blood, provided a defect in the stomach, and ulceration was the result."

Hamburger¹ stated, in an earlier work on this so-called antipepsin, that blood-serum was capable of permanently binding pepsin and preventing it from digesting protein. This inactivation of pepsin was due, however, not to a specific antibody of the blood-serum, but was due to a more specific deviation. In the course of Hamburger's work it was found that sodium chloride would completely prevent pepsin from digesting protein, and he arrived at the conclusion that this inactivation of pepsin

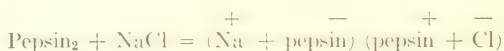
by salt and by normal serum were important factors in the action of so-called antipepsin, and that this inactivation was responsible for most of the accounts of antipepsin.

Hamburger also found that if pepsin was dissolved in an acid solution strong enough to prevent inactivation by sodium chloride, simple neutralization minus sodium chloride produced inactivation. This is apparently caused by the sodium chloride formed from interaction of acid and alkali acting in a neutral solution to cause inactivation.

The explanation is based on the modern conception of ferment action as described by Michaelis and others. It has been shown that the proteolytic action of pepsin depends on its electrolytic dissociation, and that only the positively charged pepsin ions (cations) are capable of proteolytic digestion. When hydrochloric acid is added to neutral pepsin a salt is formed, which may dissociate in one or both of two ways:



Only the cation of pepsin is active, but if sodium chloride be added in place of acid a new salt is formed, sodium pepsin, which is inactive on account of inactive anions and absence of active cations:



Hamburger suggests that a temporary achylia may be brought about by completely neutralizing the stomach acid and maintaining this neutralization, thus setting free the pepsin and rendering it permanently inactivated and deviated. He suggests that this may be done following two indications to facilitate the healing of ulcer and to prevent ulcer formation. Studies are being conducted to demonstrate and maintain continuous neutralization of the gastric contents by the use and combination of alkalies and certain foods.

This work of Hamburger discredits all attributes of antipepsin as far as preventing autodigestion of the digestive mucosa is concerned. Another point of view concerning the mechanism which prevents tissues from digesting themselves is brought forward by the Burges.

W. E. and E. L. Burge¹ studied the *rate of oxidation of enzymes* by electrolysis, using pepsin and pepsinogen, trypsin and trypsinogen, and found that both pepsin and trypsin were more easily oxidized than pepsinogen or trypsinogen. They discuss their results and the probable bearing they have on why the gastric mucosa does not digest itself. It has been shown, they say, that the mucosa of the stomach and of the intestines possesses intense oxidative properties, and it has also been demonstrated that all the ordinary digestive enzymes are easily oxidized by nascent oxygen. Based on these two facts they believe that the

¹ American Journal of Physiology, 1915, xxvii, 462.

digestive mucosa remains intact during life by rendering inactive the layer of enzyme solution immediately in contact with it. They assume, therefore, that two opposing activities are at work, *viz.*, the active enzyme within the lumen of the digestive tract attempting to digest the cells of the mucosa while the oxidative processes of these cells are rendering the enzyme inactive, and by so doing are protecting the mucosa from digestion.

Under certain abnormal conditions there is a tendency for the tissues to undergo autodigestion, and under these same conditions the oxidative processes of the tissues are decreased. Furthermore, if the blood supply be cut off from a circumscribed area of the stomach wall, pepsin begins to digest this area. It is apparent that in such cases the area is deprived of oxygen, and it is under such circumstances that gastric ulcers may arise. The fact that trypsinogen and pepsinogen are relatively difficult to oxidize explains why these substances are not oxidized in the cells of the pancreas and of the gastric mucosa during the process of secretion.

CAUSE OF GASTRIC ULCER. The main feature in the many theories advanced as to the causation of ulcer is, that there is, as has been said, a decreased resistance of certain areas of the gastric mucosa, which permits of digestion by pepsin. Burge¹ holds that in view of the fact that pepsin is easily oxidized and thus destroyed (see above), the cells of the mucosa possess oxidative properties, and that these cells become easily digested under conditions favoring the decrease of these vital properties. The Burges advance the hypothesis that normally the mucosa is not attacked by the digestive juices because the pepsin immediately in contact with the wall of the stomach is rendered inert by the oxidative properties of the cells. It is assumed *a priori* that there is a normal balance between the oxidative processes of the cells and the digestive action of pepsin, and if this balance be destroyed, as, for instance, cutting off the blood supply, this area should be digested by the pepsin and ulcer should result.

An interesting experiment with interesting results must be described. Fig. 9 represents an apparatus in which *a* is a rubber cuff holding vessels *b* and *c* in position; *d*, a piece of platinum mesh tied over the end of cylinder *b*, and *e*, a piece of gastric mucosa from a dog. The platinum mesh was covered with platinum black before tying it over the cylinder. 15 c.c. each of gastric juice (dog's) and hydrogen peroxide were made acid with hydrochloric acid to a degree shown in the original gastric juice. This mixture was poured into *b* and the whole placed in a water-bath at 38° C. The mucosa was immediately exposed to the action of gastric juice in the presence of atomic oxygen, resulting from the decomposition of hydrogen peroxide by the platinum black. After six hours the mucosa was removed from the tube and photographed.

¹ Journal of American Medical Association, 1919, LXVI, 2985.

Another preparation similar to the one described was treated the same way except that no platinum black was deposited on the mesh, hence the mucosa was exposed by the action of the gastric juice in the absence of atomic oxygen. In Fig. 10 may be seen the result of this experiment.

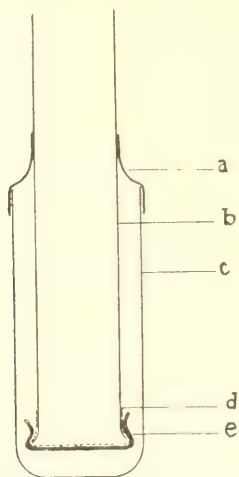


FIG. 9.—Diagram of apparatus: *a*, rubber cuff holding glass vessels *b* and *c* in position; *d*, platinum mesh; *e*, piece of gastric mucosa. (Burge.)

A is a photograph of the mucosa after the exposure to the action of gastric juice in the presence of atomic oxygen, showing no digestion of the central area. *B* is a photograph of the piece of mucosa exposed to

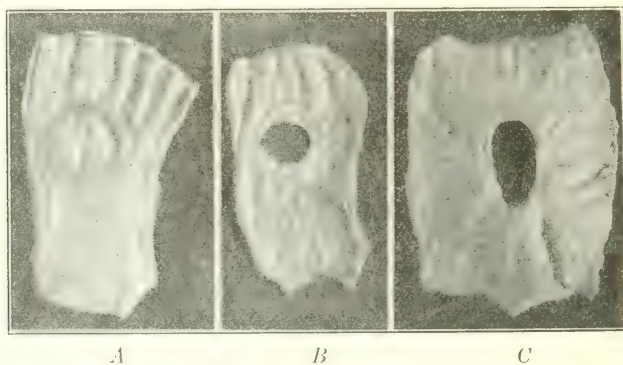


FIG. 10

the action of gastric juice in the absence of atomic oxygen. The central circular area has been completely digested with the formation of a hole, and the photograph may be compared with *C*, which is a picture of a perforating gastric ulcer.

In another place, I reviewed an earlier article by Burge, wherein it was shown that whereas pepsin is easy to oxidize, pepsinogen is peculiarly resistant. The present paper, with the bearing the earlier experiments have on ulcer, is but a continuation of their former ideas, and proves almost conclusively, I believe, that this theory has a strong foundation in fact. The question arises, If pepsin is oxidized so readily, and if it be so readily rendered so inert, why is it that we find active pepsin in gastric juice? The answer may be made, that this in no wise disproves Burge's contention, for he believes that under normal conditions that ferment which lies immediately in contact with the stomach wall is rendered inert by virtue of the oxidative processes of the cells. This, no doubt, protects the cells, and we must understand then that there is a continual protecting layer of inert pepsin surrounding the stomach mucosa during digestion, but that the pepsin is found in such large amounts that this inert pepsin in no way compares with the quantity poured out for digestive purposes, and that the great bulk of the ferment is, after all, active, and does not come in contact with the mucosa.

The experiment of the Burges is most ingenious and quite suggestive, and it will be interesting to watch further work from their laboratory.

EFFECT OF GASTRIC JUICE ON EXPERIMENTAL GASTRIC ULCER. An acute ulcer of the stomach tends to heal rapidly and in the usual manner, but when healing is arrested, then chronic ulcer appears, and it is this persistent tendency of chronic gastric ulcer to remain unhealed that has so far baffled solution. The normal gastric processes cannot, therefore, exert much deterring influence on the healing of an ulcer, but, in the case of chronic ulcers, it is apparent that the digestive processes are not conducted normally. It is well known that all patients so afflicted suffer from attacks of food retention due either to pylorospasm or to muscular inefficiency, and the majority of cases are associated with hypersecretion and hyperacidity. Clinicians have believed, without any direct evidence to support this view, that the gastric juice played an important role either in the irritation of an ulcer, or in its propagation. Katzenstein has, as I have mentioned elsewhere, contended that the ferment of the gastric juices was the chief destructive agent in the absence of anti-ferment, but Bolton¹ maintains that it is the acid of the gastric juice, and bases this belief on his experiments. His view as expressed by him may be put down as follows:

1. The normal gastric juice is able to attack the gastric mucous membrane which has been damaged or devitalized, without actual death of the cell.

2. This property it owes to hydrochloric acid acting as a protoplasmic poison, and thus completes the death of the tissue.

¹ *Journal of Pathology and Bacteriology*, 1915, *vol.* 143.

3. The ulceration produced in the presence of a hyperacid juice is much more extensive than that produced when the gastric juice is normal.

4. Acute ulcer is more easily and quickly produced in the digesting than in the resting stomach, and is more extensive in the former than in the latter.

5. Motor insufficiency of the stomach, leading to undue retention of food, delays the healing of an ulcer for at least twice the normal time, owing to necrosis of the granulation tissue of the base of the ulcer by the prolonged action of HCl in the gastric contents.

6. For the same reason healing is prolonged by a diet which causes considerable secretion of gastric juice and leaves the stomach slowly, while repair is hastened by the opposite kind of diet.

In the present article, Bolton's experiments refer particularly to the effect of hyperacidity alone and combined with motor insufficiency upon the healing of ulcer, and to the effect of hyperacidity upon the mucous membrane of the stomach.

1. *The Effect of Hyperchlorhydria upon the Healing of Gastric Ulcer.* Monkeys were used, and ulcers were produced by a gastrototoxic serum. The gastrot toxin is abstracted from the serum and becomes fixed on the tissues, particularly the cells of the mucosa. The affected portion of the mucous membrane is attacked by the gastric juice and a slough is formed, which gradually separates with the formation of a clearly punched-out ulcer, extending to various depths in proportion to the strength of the serum. The ulcer is formed in about four or five days. The stages in the healing of such ulcers may be described as follows: "When the sloughs have separated from the edges, but before they have completely separated from the base of the ulcer, the glandular cells at the edges begin to proliferate and cover the raw surface with a single layer of flat cells. These cells become cortical in shape, and from them simple tubes, which eventually form new glands, bud off to grow down into the granulation tissue. The base of the ulcer becomes covered with granulation tissue when all the sloughs have separated, and the single layer of flat epithelial cells at the periphery grows out over the tissue, and by about the twenty-first day has completely covered it. During this time the edges of the ulcer are being drawn nearer together by the contraction of the newly formed fibrous tissue in the base of the ulcer, so that an increasingly smaller surface remains to be covered. The epithelial cells covering the base now send out buds in the shape of simple tubes which proliferate in the underlying cellular stroma, and so the new mucous membrane gradually thickens as the glands become freely formed."

Hyperchlorhydria was produced by introducing into the fasting stomach a solution of HCl of varying strengths. The effects of hyperchlorhydria upon extension of the ulcer were variable, and in no case was there any regular extension of the ulcer. If the HCl is of a certain

strength, cell death results, but, when once the ulcer is formed, the gastric cells at the edge of the ulcer remain healthy and no regular extension of the ulcer occurs. The extension of an ulcer, under these conditions, is due to the persistence of the original cause of the ulcer and not to the gastric juice itself. When the gastric juice was made hyperacid, there was a definite delay in the healing of an ulcer, amounting to four weeks beyond the normal time. The cause of the delayed healing was the necrotic condition of the base of the ulcer. The acid killed off the connective tissues of the base, though unable to attack the gastric cells at the edge of the ulcer; the superficial layer of the base was rendered necrotic and, hence, epithelial growth over the base was retarded.

Bolton believes that, in the human being, hyperchlorhydria would produce a greater effect than the same degree of acidity induced in the monkey's stomach by pouring acid into it at certain times.

II. *Effect of Hyperchlorhydria together with Motor Insufficiency upon the Healing of Ulcer.* It has been shown that motor insufficiency of itself can materially delay the healing of an ulcer, and the prolonged action of hydrochloric acid was held responsible. Motor insufficiency was produced by artificial duodenal obstruction. The results of experiments with motor insufficiency and hyperchlorhydria combined, when compared with the results obtained with hyperacidity alone, show that the ulcers were larger and less disposed to healing than those in which hyperchlorhydria alone was produced. The cause of the delayed healing was necrosis of the base of the ulcer. Bolton is quite certain that if these effects are seen in animals, they must be far greater in man.

III. *Effect of Hyperchlorhydria upon the Gastric Mucosa.* Certain well-marked changes were found to occur with solutions of HCl.

(a) *Irritant Effect.* This was manifested as a chronic inflammation of the mucous membrane. The stomach contained a good deal of mucus. punctate hemorrhages were seen in the advanced cases, enlarged lymph follicles could be seen under the mucous membrane scattered about the stomach like seeds. Slightly depressed rounded patches were sometimes observed surrounded by a well-defined rim of normal tissue. Microscopic examination showed that the gastritis was either a more or less diffuse condition or that it was localized to patches surrounded by perfectly healthy mucous membrane. Bolton gives full description of the microscopic findings which I omit. It may be mentioned that the gastritis does not affect the healing of ulcer, nor does it affect the movements of the stomach.

(b) *Necrotic Effect.* Apart from the irritant effect of the acid, hydrochloric acid in certain strengths is able to kill a tract of mucous membrane of various depths and by continuous administration a wide-spread ulcer may be produced.

To resume then; Bolton's work has demonstrated that gastric juice is concerned in the irritation as well as in the chronicity of a gastric ulcer,

due primarily to HCl. The acid is usually but a factor in the irritation of ulcer, but when of a percentage 0.39 or upward continued with motor insufficiency, it may be the actual cause of ulcer. Ulcers are more likely to spread when there is hyperacidity and motor insufficiency. In man, ulcer, hyperacidity, and gastritis are generally associated, and it has been shown by Bolton that hyperacidity precedes the gastritis and causes it. The ulcer, then, is not the cause of the gastritis.

GASTRIC JUICE IN GASTRIC AND DUODENAL ULCERS. It will be more or less of a shock to clinicians to learn that, although it is commonly stated that in gastric and duodenal ulcer, hypersecretion and hyperacidity is the rule, no one has reported any definitely controlled experiments to prove this contention. But so we are informed by Hardt,¹ To study this problem, experimental ulcers were produced by injecting streptococci after the method of Rosenow, the *Bacillus coli* being rejected, as no ulcer could be found after intravenous injections of this organism, according to the technic of Steinharter.

There were striking variations in the secretion-rate and acidity following test-meals, but there was no change in the concentration of the acidity which could indicate the presence of an ulcer in the experimental animals. Both before and after operation the acidity ranged from 0 to 0.55 per cent. Only two, of eight dogs experimented with, showed hypersecretion, and this may be due to a local hypersensibility of the gastric mucosa or may be the result of the absorption of toxins from the ulcer and a stimulation of the vagus fiber. When the gastric ulcer is extensive, Hardt suggests that hypersecretion may result from gastritis (see above).

The important conclusion one arrives at from Hardt's work is, that gastric and duodenal ulcers may, or may not, result in a continuous hypersecretion, but that there is no hyperacidity. Is one justified in applying this result to man? It must be apparent that many factors have to be considered when gastric studies on animals are undertaken. There are so many psychic factors influencing the chemistry of a dog's stomach that experiments must be controlled in every direction before conclusive statements can be made. Pawlow has shown, in dogs, what effects slight disturbances in the laboratory itself exercise, and one cannot read his results too closely when one appreciates this. Hence I do not feel that clinicians should necessarily abandon the well-grounded belief that hypersecretion and hyperacidity are frequently met with in ulcer cases, despite the admirable work of Hardt which tends to prove that hyperacidity is not found as the result of ulcer.

BACTERIAL STUDIES IN EXPERIMENTAL GASTRIC ULCER. The staphylococcus organisms obtained from a case of septicemia in man, were injected, together with acetic acid, into the pyloric end of the stomach by

¹ American Journal Physiology, 1916, xl, 314.

Steinharter,¹ and typical ulceration resulted. Steinharter believed that the staphylococcus is responsible for certain cases of gastric ulcer in man, and he says, "If by some means (through an erosion or trauma, etc.) a hyperacid gastric juice enters the tissues of a limited area of the stomach wall, and the staphylococcus of proper virulence (for example, from the appendix) finds lodgement there, it does seem quite probable that the necessary conditions used in producing the experimental ulcer would be duplicated." (See Hardt for refutation of this work.)

Celler and Thalheimer² have made bacteriological studies of the organisms found in human gastric ulcers removed at operation, and have succeeded in isolating streptococci, yeast and various types of bacilli. The streptococci were cultured and were injected into rabbits. Efforts to repeat Rosenow's work were scrupulously made according to Rosenow's method. Certain defects in the gastric mucosa resulted, but difficulty arises in determining whether these are true ulcers. By injecting bacteria intravenously, only superficial lesions were produced, which are not analogous to chronic human gastric ulcer. Injections into the branches of the gastric artery resulted in shallow indurated defects which might be considered ulcerations but which were found to be completely healed in a relatively short time. It is true that an anhemolytic streptococcus is found constantly in human ulcers, and it would be an argument in favor of the role this organism plays in the chronic nature of ulcer, were it not that the bacteria are found only superficially, no great number being found in the depth of the ulceration.

The authors refer to the work of Cushing and Livingood which showed that although, normally, the stomach contains no bacteria, organisms may be introduced with the food, and are removed mechanically when the ingestum is removed. Bacteria cannot adhere to normal mucous membrane, but the possibility of organisms remaining beneath the degenerating lining of the ulcer, because of favorable mechanical or structural conditions, must be borne in mind. Celler and Thalheimer are not convinced of the role streptococci play in the causation of ulcer, or in the prevention of healing, although they recognize the suggestive fact that such organisms are constantly present in all gastric ulcers, and may be a factor the importance of which further experiments must determine.

EXPERIMENTAL GASTRIC ULCER. Wilensky and Geist³ contribute some work with the experimental production of gastric ulcer, injecting bacteria into defects in the mucosa of stomachs of cats. The bacteria were cultured from human gastric ulcers excised at operation. Repeated laparotomies were made on the experimental animals in order that the condition of the defect might be observed, and when the ulcer showed a tendency to heal, it was infected again with the same strain of

¹ Boston Medical and Surgical Journal, 1916, clxxiv, 678.

² Journal of Exper. Med., 1916, xxiii, 791.

³ Journal of American Medical Association, 1916, lxvi, 1382.

bacteria. Their results demonstrated (nine animals) that the presence of the organisms found in human gastric ulcers has no appreciable effect either in giving to the experimentally produced defects characteristics of the chronic indurated ulcer, or in retarding their healing, a refutation of the claims of Rosenow.

ADRENALECTOMY AND GASTRIC ULCER. The ulcers found in animals following the removal of the adrenals are considered by Mann¹ to develop during the moribund period. They are true acute ulcers penetrating to the muscularis mucosa with a total loss of epithelium. They are apparently peptic ulcers, forming at the site of local hemorrhages in the gastric mucosa, and appear to develop only in an acid medium.

Finzi² believes that changes in the circulation followed extirpation of the adrenals and he was able to prevent ulceration by giving to the animals subcutaneous injections of adrenalin. In five cases of human gastroduodenal ulceration he found notable changes in the adrenals, namely, chronic thickening of the capsule, nodular hypertrophy, embolism, fatty degeneration, congested and multiple hemorrhages.

Gastric Cancer. A paper by Schütz³ in purpose similar to the excellent article by Smithies quoted last year, *PROGRESSIVE MEDICINE*, 1915, page 55, contains the conclusions arrived at from the study of 387 cases of malignant disease of the stomach. Schütz believes that alcohol accounts for carcinoma being found more frequently in men in his series; 68 per cent. were male and 32 per cent. females. The youngest patient was a woman of twenty-six; 15 between thirty and forty; 103 between fifty and sixty; and 13 were over seventy. No free hydrochloric acid was found in 90 per cent. of the 197 tested. This represents the highest percentage in any series yet published and emphasizes the importance of subnormal acidity in cancer. In none of the number was there hyperacidity, and, in the 17 with free acid, it was well within modest range. Schütz emphasizes, however, that anacidity can be regarded as a sign of cancer only when it is a question of early differentiation of cancer. He found anacidity in only 7.4 per cent. of 830 cases of non-cancerous stomach affections, but anacidity is liable to accompany chronic infectious diseases, such as tuberculosis, and certain metabolic derangements (uric acid diathesis). The anacidity here is not the consequence of the concomitant anemia, with the exception of pernicious anemia and leukemic states. Deficient production of hydrochloric acid seldom occurs with anemia, even extreme. The anacidity is evidently the result of some profound derangement, probably from the injurious influence of certain products of the abnormal metabolism. It is possible that a similar profound upset is responsible for the anacidity in gastric cancer, instead of local conditions. Skray found, in some cases of simple

¹ *Journal of Exper. Med.*, 1916, xxiii, 203.

² *PROGRESSIVE MEDICINE*, December, 1914, p. 26.

³ *Abstract Journal of American Medical Association*, 1916, lxvi, 1062.

achylia and subacidity, that hydrochloric acid appeared in the stomach content after meat was added to a test-breakfast, while with cancer no acid appeared. Schütz found, in 46 cases, that the stomach content had a putrid odor, a reliable sign of a neoplasm undergoing decay at some part. In 57 per cent., the evacuations of the stomach proceeded normally or overhastily. In 130 cases the Röntgen findings were suggestive of malignant disease in 100, but in 84 of these the diagnosis was certain otherwise; in 30 the Röntgen findings testified against cancer, but the findings otherwise in 25 cases rendered cancer certain. In 16 cases the cancer was disclosed by the Röntgen findings alone. Lactic acid was demonstrated in 33 per cent. exclusively with cancers obstructing the outlet. His conclusion is that the diagnosis of malignant disease of the stomach is, in its earliest phases, practically impossible. We shall succeed in diagnosing it more frequently when we make a practice of applying the various tests early in stomach trouble of any kind.

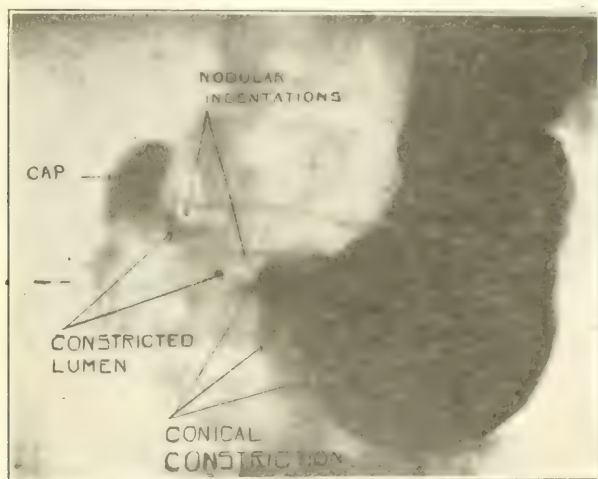


FIG. 11.—Typical carcinoma. (Cole.)

X-RAY DIAGNOSIS OF GASTRIC CANCER. Throughout Cole's¹ paper one is impressed with the author's conviction of the reliability of x-ray in diagnosing gastric cancer. He writes emphatically to the effect that "The time has come, therefore, when a man need not remain in doubt for a single day as to whether he has gastric cancer or a pre-malignant area of induration which may at any instant become malignant. If either of these lesions is known to be present, a roentgenographic examination is of inestimable value in determining whether surgical procedure is necessary, and if so, whether a radical operation is indicated or only a palliative procedure is possible." He includes indurated gastric ulcers

¹ New York Medical Journal, July 3, 1915.

under the term cancer of the stomach, for, he says, it is the consensus of opinion among surgeons and to a great extent among diagnosticians, that indurated ulcers are the source of cancer, and he regards indurated gastric ulcers as cancerous until they are proved otherwise by microscopic examination.

When the gastric walls are invaded by new growth, they fail to expand to their normal dimensions. Since similar "filling defects" are seen in benign conditions, this differentiation must be especially noted.

Fig. 11 is a case of malignancy, and Fig. 12 one of non-malignancy, and Cole gives the following table of comparative data.

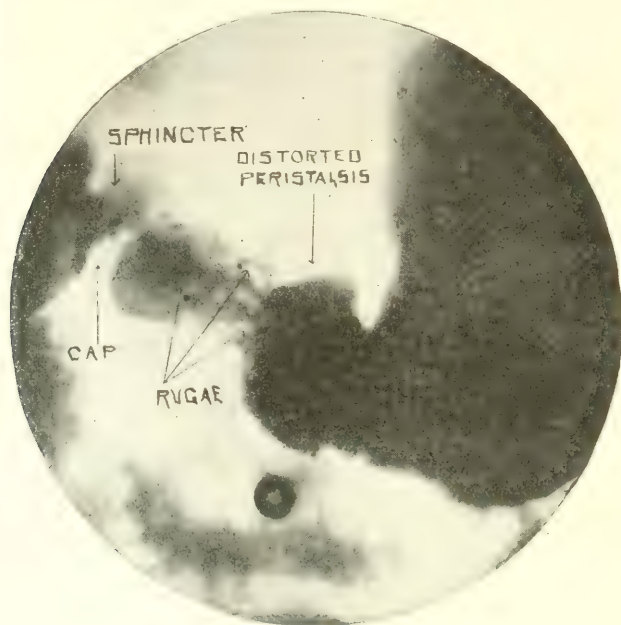


FIG. 12.—Typical spasm. (Cole.)

MALIGNANT.

Rugæ are absent.

Lumen of constricted area is constant in size, shape and position.

Peristaltic contractions are absent in involved area.

Lumen is encroached upon by nodular growth projecting into the stomach wall.

Line of invasion is characterized by nodular indentations similar to finger-prints in putty.

NON-MALIGNANT.

Rugæ show with unusual distinctness and run obliquely or transversely.

Lumen varies in size but never completely relaxes or contracts.

Peristaltic contractions in involved area are unusually wide and shallow.

Lumen is diminished by a contraction of the muscular coats of the stomach without the projection into the lumen of localized areas.

Line of invasion may be sharp and clear cut or finely serrated by the rugæ coming to the surface, but shows no nodular indentations.

Cole classifies gastric carcinomas as of several types, according to the form, extent and location of the erosion as observed roentgenologically. The following is a verbatim copy of his article.

"Type I. The lumen of the stomach may be encroached upon by a nodular growth in the wall of the viscus, from which projections extend into the normal tissue at the line of invasion, like the peninsulas or islands (Fig. 13). This gives a peculiar appearance to the fluid cast of the stomach, suggesting finger-prints in a piece of putty.

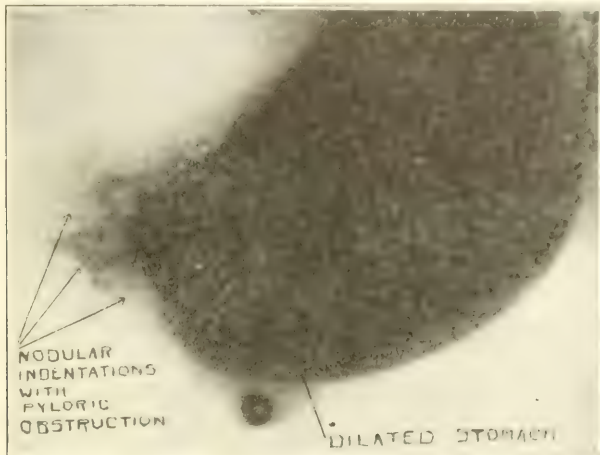


FIG. 13.—Pyloric obstruction. Surgery for palliation indicated. (Cole.)

"Type II. The growth may be formed of one large, fairly smooth mass, projecting into the lumen from one wall or curvature of the stomach (Fig. 14). The uninvolved portion may functionate in a normal manner, and there may be no obstruction to the passage of chyme. At an earlier stage, when the growth may or may not be malignant, it appears as a small constant induration (Fig. 15), which so closely resembles a broad peristaltic contraction that it is necessary to use great care in differentiating the two phenomena; but it will be seen in studying a series of roentgenograms, that the induration does not progress pylorusward nor relax during diastole. These cases are readily detected at an exploratory laparotomy, and are amenable to surgical procedure. But the surgeon cannot determine their malignancy with any greater degree of certainty than the roentgenologist. He does not know whether he has prevented a carcinoma by excising an indurated ulcer or removed an early carcinoma until he receives a pathological report after the specimen has been examined microscopically.

"Type III. The growth may be annular, involving the entire circumference of the gastric wall. An extensive involvement may reduce the diameter of the lumen to one-eighth inch or even entirely obliterate it.

(Fig. 9). If the röntgenograms of a series are matched over each other, it will be seen that the constricted area is constant in size, shape, and

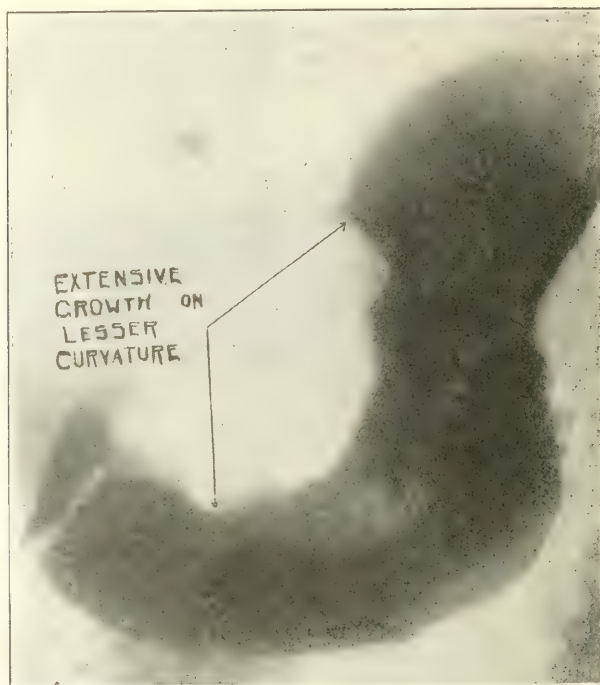


FIG. 14.—Carcinoma on lesser curvature, too extensive for removal. No obstruction; no occasion for gastro-enterostomy. (Cole.)

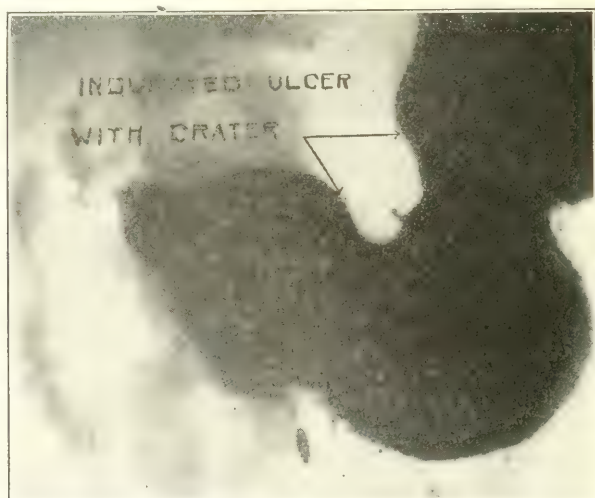


FIG. 15.—Precarcinomatous area on lesser curvature. Surgery indicated for complete cure. (Cole.)

position. Where the growth joins the normal tissue, the line of invasion may have a worm-eaten appearance, with overhanging edges (Fig. 10), or it may be conical or funnel-shaped, the flaring edge of the conical area corresponding to the line of involvement, while the apex of the funnel terminates at the most constricted area.

"Type IV." Small annular growths, which are found at the extreme end of the stomach, are usually of the adenocarcinoma type, and freely movable (Fig. 16). In two cases which presented a typical roentgenographic picture of this type of involvement, the growth was considered benign by the surgeon at the time of operation. In one of these cases, a gastro-enterostomy was performed, and the patient died later of gastric carcinoma. The other was a case diagnosed and reported by Doctor George as carcinoma of the pylorus. At operation the surgeon excised



FIG. 16.—Annular pyloric carcinoma. Surgery indicated. (Cole.)

the affected tissue, simply because it was easy to remove, believing it to be an ulcer. The surgeon and pathologist both considered it benign on gross examination. Microscopic examination, however, proved that it was malignant. In spite of the fact that the microscopic findings proved its accuracy, the case has been cited as an example of the absurd presumption of a roentgenologist's diagnosis.

"It is a fortunate circumstance when a marked narrowing of the gastric lumen, causing retention and dilatation, results while the growth is still small. Such lesions which cause symptoms early, while the growth is freely movable, offer a good opportunity for surgical cure. In one case of this type the gastric secretions were so nearly normal that the patient was kept under observation in the hospital for six weeks before an operation was performed.

"Type V. The scirrhus carcinoma, which involves a considerable area without projecting appreciably into the gastric lumen, is the type of growth most likely to escape detection by röntgenological methods. The absence of the peristaltic rings in the involved region is the first clue by which this lesion is identified. That part of the stomach infiltrated with carcinomatous cells is less pliable than the normal gastric walls, and the peristaltic rings are therefore obstructed in their progression pylorusward when they reach the area of infiltration. An absence of the deep, angular sulcus on the lesser curvature is of great importance (Fig. 17). As a simple demonstration of what happens, a string may be tied around an inflated rubber tube where a small patch has been applied. The patched portion will not be creased by the string like the rest of the tube.

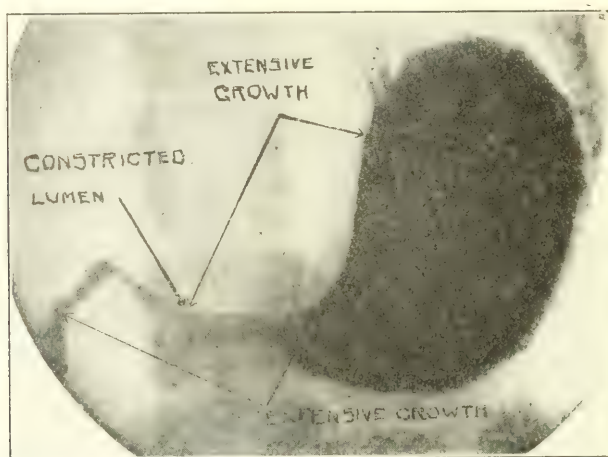


FIG. 17.—Pyloric obstruction. Growth too extensive for removal, or for gastroenterostomy. (Cole.)

"Another finding characteristic of scirrhus involvement consists of slight irregularities in the wall of the stomach, visible only upon close inspection, which present an absolutely identical contour in all the röntgenograms, as can be seen by matching the röntgenograms over each other. Such growths occur frequently on the lesser curvature. Small constant creases on the greater curvature near the pylorus, which very closely resemble a peristaltic sulcus, frequently call one's attention to the extensive lesion on the lesser curvature which might otherwise escape detection. If the involvement is extensive and the stomach considerably contracted, the non-pliability of the gastric walls causes a dilatation of, and retention in, the lower end of the esophagus, a phenomenon to which Schmieden calls particular attention. It is important to differentiate this condition from the Haudek niche, caused by a perforating gastric ulcer of the lesser curvature. (See Diverticulum of the Stomach.)

"*Type VI.* In many cases, particularly those in which a roentgenographic examination is not made until the patient presents classical symptoms of cancer of the stomach, there is such complete obstruction that even the hair line of bismuth, connecting the lumen of the stomach with the small intestine is not visible. In these cases the apex of the cone or funnel-shaped constriction indicates where the constriction originated (Fig. 13). Unfortunately, a large percentage of the carcinomas found roentgenographically belong to this group; and this will continue to be the case until the laity and profession realize that, in order to detect carcinomas at an early stage, all patients past forty years of age with even slight gastric symptoms, must be examined roentgenographically if the lesion is to be detected at a stage when a recognition of the condition is still of some value to the patient.

"*Type VII.* The roentgenographic picture of a saddle-shaped ulcer is more graphic than words can describe (Fig. 14). The affected area may conform to the lines of an English saddle, having more or less a flat surface, with flaps extending down on the anterior and posterior surfaces of the stomach, or it may be deep, with a high pommel and back, like a typical McClellan army saddle. While such lesions are usually described surgically as gastric ulcer, all those I have seen proved malignant upon microscopic examination. This type of involvement causes no obstruction to the passage of chyme and no gastric retention. Indeed, such a stomach usually evacuates itself with uncommon rapidity, either on account of the diminished hydrochloric acid, or because adhesions interfere with the normal function of the pyloric sphincter."

Inoperable cancer he divides into two groups: (1) Lesions too extensive to allow even a gastro-enterostomy; (2) gastro-enterostomy possible but not indicated.

The first group is illustrated by Fig. 17, the second by Fig. 14.

The operable cases are divided into those for whom operation is performed for palliative relief, and those for surgical cure or prevention. Cases which offer much from the surgical side are those where there is a small annular growth at the pyloric end of the pars pylorica, freely movable and demanding immediate operation regardless of gastric symptoms. Such cases develop complete pyloric obstruction rapidly, unless surgery intervenes (Fig. 16). Another class of case is that of indurated ulcer which may or may not be malignant.

Another very able paper is that by Carman¹ who is also impressed by the great value of the x-ray in diagnosing cancer, particularly early carcinoma.

LABORATORY TESTS FOR CANCER. ALBUMIN TEST. Katanetson² studied the Wolff-Jungmans reaction in 21 cases of achylia, and in 14

¹ American Journal of Medical Sciences, 1915, cl, 625.

² Abstract Journal of American Medical Association, 1915, lxxv, 836.

with various degrees of acidity, but all without blood in the stomach contents. He did not practise lavage before the test-meal. In 9 cases of malignant achylia with complete absence of hydrochloric acid and total acidity not exceeding sixteen, or total anacidity as occurred in 7 cases of this group, he found the albumin index between 200 and 400. In 10 cases of benign achylia, the index ranged from 20 to 30. In 2 cases of doubtful achylia, cancer probable, it was 100 and 400. The reagent used is a mixture of 0.3 part of phosphotungstic acid; 1 part of hydrochloric acid, 20 parts of alcohol and water to 200 parts. Stomach content is placed in a set of beakers and diluted from 0.25 to 10 per cent. In each beaker 1 drop of reagent is superimposed on the diluted content. The index is the dilution in the first beaker in which no ring forms at the point of contact. The albumin index is thus the figure representing the dilution; 10, 20, 40, 80, 100, 200, or 400. In Katznetson's cases, he thus found the albumin index in 9 cases of gastric cancer from 200 to 400 (average 355). In his 10 cases of benign achylia, it was from 20 to 80 (average 55). Hence it seems that an albumin index below 80 speaks for benign conditions, above 100 for malignant forms of achylia. As the test is so very simple, it must be considered an extremely valuable method for differentiating between malignant and benign achylia. Cases in which even small amounts of the hydrochloric acid are present are not suitable for this test, as there is liable to be considerable albumin in the stomach content. The index ranged from 100 to 400 in 14 patients with different proportions of hydrochloric acid in their stomach content, although cancer could be positively excluded.

Zoeppritz¹ points out that the presence of dissolved albumin in the fasting stomach does not decide between ulcerative and non-ulcerative processes, but the absence of albumin renders the assumption of malignant disease highly improbable. Stagnation of stomach content and lack of the normal acid favor the appearance of albumin in the stomach washings, but do not influence its production. Albumin may sometimes be found in the clinically normal stomach, but it occurs more frequently with chronic gastric disease. His tabulated records of 48 operative cases of gastric cancer showed a positive response to the Esbach test in all but 8 cases, and there was no free acid in 7 of this group and very little in the remaining case. His tables show, further, a positive reaction in 14 of 21 operative cases of gastric ulcer, and 5 of 6 without an operation; also in 5 of 6 operative cases of chronic gastritis, and in 8 of 8 non-operative cases; in 4 of 7 other operative stomach affections, and in 5 of 5 non-operative; in 14 of 16 operative abdominal affections, and in 12 of 12 in which no operation was attempted. In 1 case extensive carcinoma in the submucosa had irritated the mucosa and caused secretion of mucus and nuclein, which gave the positive albumin reaction, although

¹ Abstract Journal of American Medical Association, 1915, lxx, 2263.

there was scarcely any ulceration, and this was close to the gaping pylorus. The various groups are tabulated in detail and the reactions compared with other tests for cancer. In 135 cases of gastric cancer at Kiel, occult or visible blood was found in 95 per cent., there was emaciation in 90 per cent., anacidity in 89, dissolved albumin in 83, lactic acid in 67, long bacilli in 64, and a palpable tumor in 64 per cent. The albumin reaction was positive, if at all, very soon after the first symptoms appeared. The test for albumin is simple and easy if the stomach motor function is normal, but with impaired evacuation it is a tedious matter to rinse the stomach clean, and the slightest erosion of the stomach wall nullifies the findings of the test.

Paus¹ has applied Salomon's test for albumin in stomach content of 6 cases of known cancer, in 5 of gastric ulcer, and in 9 persons free of gastric symptoms. The findings are tabulated. The response was positive in only 5 of the 6 cancer cases. With ulcer the reaction was always slight or negative, so that a pronounced reaction is good presumptive evidence of cancer, but when this occurs the symptoms usually point to cancer without necessity for any test.

MIOSTAGMIN REACTION. Wissing² devotes considerable space to the technic of the test, the errors to avoid, the precautions to take, and many details concerning the method which is of little interest to us here. His researches lead him to believe the test is not specific for carcinoma, since other diseases give positive reactions. Happily, the clinical differentiation between these non-malignant conditions and cancer is easily made, so that this objection may be of little practical importance. The morbid process, apart from carcinoma, which furnished positive reactions in 350 individuals without a sign of cancer were:

1. All febrile states, the reaction disappearing a few days after defervescence.
2. Practically all pregnant women, in the last three or four months, give miostagmin reactions, but these disappear two weeks after parturition.
3. Cardiac decompensation.
4. Hepatic cirrhosis and icterus.
5. Advanced pulmonary tuberculosis.
6. A few cases of diabetes mellitus. Acidosis seems to play no role in the production of the test.
7. A few cases of polyarthritis chronica rheumatica. Most of these cases were receiving salicylic acid, but this apparently exerted no influence. In general the patients were febrile.
8. A few cases of chronic nephritis and uremia.

As Wissing says, these cases could scarcely be confused with carcin-

¹ Abstract Journal of American Medical Association, 1910, lxxx, 994.

² Berl. klin. Woch., 1915, p. 998.

noma, with the possible exception of icterus, which gives a positive reaction whether the causation of the jaundice be malignant or benignant processes. In benign cases of jaundice the reaction disappears when jaundice disappears, while in malignancy the test is persistently positive.

Of much more importance is the fact that there are many diseases resembling carcinoma in which there is no miostagmin reaction, for example, benign tumors, gastric ulcer, chronic gastritis, enteritis, colitis, and certain syphilitic manifestations. Here the test would seem to be possessed of much value, since negative reactions are the rule.

Balcerek¹ studied the course in connection with the miostagmin reaction in 3 cases of sarcoma and 43 of cancer, as also in 135 patients with various other affections, the ordinary cases of a general hospital. The response was negative in these 135 miscellaneous cases, and negative also in the few cases of cancer displaying a tendency to scirrhus. But it was distinctly positive with all the cancer patients, and gave the sole clue to the successful treatment in a number of dubious cases which he describes in detail. A positive reaction was obtained further in 4 cases of nephritis in the uremic stage, in a case of pulmonary tuberculosis, and in one of a valvular defect. In these last 2 cases, the test was made at the height of menstruation, which probably may be the explanation of the positive puzzling reaction. In a case of intercurrent pneumonia with cancer of the pancreas, the response was negative, but veered to positive as soon as the pneumonia subsided. Effusion and transudate did not always give a positive reaction with cancer when the serum findings were strongly positive.

AMINOLYTIC FERMENT IN GASTRIC CONTENTS IN CARCINOMA. When we have reviewed the well-known methods of examination of the gastric contents, the best we can say of their value in diagnosis of gastric carcinoma is, that they show that gastric chemistry in this condition varies in many particulars from the normal. Thus speaks Halpern² and forthwith proceeds to search for another ferment, an amidase, an enzyme which is able to split monoamino acids into formic acid and amino groups. Formic acid has been found in many animal fluids, in urine, in meat juice, in sweat, and in the gastric contents of the shark. Seeking to learn more of the role that the acid plays as an intermediary product of sugar metabolism, Halpern was surprised to find that in gastric carcinoma this acid might be found.

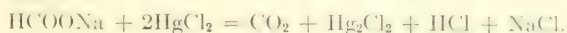
A test-meal was given and the contents were placed in the oven for twenty-four hours, and then tested for formic acid. This method being unsuccessful, amino acids were added to the contents, in the supposition that such an aminolytic ferment might not be able to break up the higher

¹ Abstract Journal of American Medical Association, 1916, lxvi, 67.

² Mitt. aus den Grenzgeb., 1915, xxviii, 709.

protein molecule, but might be able to attack the lower amino acid. Glycocoll or alanin was used, 0.163 gram being added to 20 c.c. of gastric juice. This furnishes 0.1 gram of formic acid.

The technic is as follows: The stomach is washed out in the morning and the customary test-meal given. The gastric contents are filtered, and in a sterile Erlenmeyer flask are placed 0.163 gram of Kahlbaum's commercial glycocoll. The flask is shaken, covered with toluol, stoppered, and put in the oven. After twenty-four hours, the contents are poured into an 800 c.c. Kjeldahl flask; 10 c.c. of 50 per cent. phosphoric acid (Kahlbaum's) are added to liberate formic acid, this latter being distilled with steam. The process is finished when 10 c.c. of the distillate, after phenolphthalin addition, shows permanent reddening with 1 drop $\frac{N}{10}$ NaOH. The whole distillate is neutralized, and to it are added 15 c.c. of a solution containing 200 grams of sublimate, 300 grams of sodium acetate, and 80 grams of sodium chloride in a liter of water. The whole is heated for four or five hours in a boiling water-bath. The resulting change is expressed in the following reaction:



To the fluid 2 or 3 c.c. of concentrated hydrochloric acid are added which dissolves all the substances precipitated by sublimate, but not the calomel. This is filtered in a Gooch crucible, the calomel remains, is dried at 100°, then is desiccated, and weighed; 1 gram of calomel corresponds to 0.097 gram of formic acid.

In a series of 17 cases, formic acid was seen in every instance of carcinoma, but not in the benign conditions. In the positive cases the amount was 0.03 to 0.2 gram per 100 c.c. of gastric juice; in the negative cases, 0.001 to 0.002. These low values were considered negative.

Halpern believes that the ferment, amidase, is probably a secretory product of the cancer cell, and although at present he has found no case other than carcinoma furnishing this ferment, his cases are too few to admit of definite conclusions.

ABDERHALDEN REACTION IN CANCER. Levin has previously written that the Abderhalden dialysis method cannot be considered as yet of real value, since it is positive in nearly 50 per cent. of non-cancerous patients. Using the quantitative method devised by Van Slyke and Vinograd, Levin and Van Slyke¹ now believe that, with the quantitative method, less difference can be detected between the reactions obtainable with normal and supposedly specific serums. They conclude, however, that the diagnostic value of the Abderhalden reaction in cancer is doubtful, to say the least, and they emphatically state that for the present, the method belongs to the research laboratory and not to the clinic.

¹ Journal American Medical Association, 1915, lxx, 945.

velops symptoms similar to those produced by the original lesion, such symptoms being persistent and unrelieved by any medication, it is fair to assume that an ulcer has occurred in the region of the anastomosis. It is most characteristic of a gastro-jejunal ulcer if, together with symptoms resembling those produced by the first lesion, there is pain to the left of the midline and below the umbilicus. Much assistance in diagnosis may be expected from the röntgenologist, and it is this aspect of the subject that the authors have under discussion.

After gastro-enterostomy, the following conditions are found normally:

1. The opaque meal passes freely from the stoma.
2. No retention is present in the stomach from a six-hour meal.
3. The duodenum is not dilated.
4. The stomach is usually small.
5. Peristalsis is not overactive.
6. The gastric contour in the vicinity of the stoma is not deformed, except for an occasional slight dimpling at that point.
7. The efferent limit of the jejunum is neither narrowed nor markedly irregular in outline.
8. Extensive adhesions about the stoma are uncommon and the stomach is moderately mobile.
9. The stomach is not deformed, and has no tendency to hour-glass contraction or spasticity.

In nearly all cases of gastrojejunal ulcer there are definite röntgenologic indications of an abnormal condition, and there are, in many instances, more or less direct signs pointing to the location of the trouble. The most direct evidence is marked deformity about the stoma, although in other cases the opposite of the nine normal findings have been found. Carman and Balfour wisely state that a correlation of röntgenologic and clinical data is required for the correct diagnosis. A case in point occurring in my work, was a patient, who, six months after a gastro-enterostomy for gastric ulcer, began to have, as Carman and Balfour state, recurrence of symptoms similar to those produced by the initial lesion. Stool examinations failed to discover blood, the stoma was patulous and there seemed to be no reason to suspect that the anastomosis was not functioning as it should. Attention to diet and certain medical measures have successfully combated the symptoms.

Benign Proliferation of Glands in the Stomach. De Jong¹ describes in detail 4 cases in which there had been more or less serious disturbances of the stomach. In 3 the normal glands near the pylorus had proliferated, narrowing the lumen. In the fourth case there was a lump of aberrant pancreas tissue obstructing the lumen. The assumption of malignant disease had been amply justified by the disturbances, and the discovery of the absolutely normal microscopic tissue in the tumors was a

¹ Abstract Journal of American Medical Association, 1916, lxvi, 392.

great relief. One patient was a woman aged thirty-eight, and she had had stomach trouble for over two years, with much pain and emaciation. There was also a history of a period of similar trouble at eighteen. The stomach sagged and was much dilated. The lumen at the pylorus was obstructed by a ring of enlarged Brunner's glands, and complete recovery followed resection of the pylorus and gastro-enterostomy. Nothing was found to suggest an inflammatory process. In a second case the enlarged glands formed a single tumor in the duodenum. A boy aged twelve succumbed to sarcoma of the tibia but shortly before death complained of severe abdominal pain, explained by perforation of the ulcerated and enlarged glands. The third patient was a man aged twenty-eight who died from perforating ulcers, two in the stomach and two in the duodenum. One of the former had developed on an enlarged gland. In all three the proliferating gland tissue was apparently entirely normal. The condition is not like that of congenital hypertrophy of the pylorus, but its cause is fully as much of a mystery as the latter. Both are primary affections. He does not know of any similar cases on record in which the connection with gastric disturbances was ascertained during life, although Alsleben has reported some similar findings in cadavers. De Jong recently discovered a small cyst at the pylorus in the cadaver of a man aged forty-six, but there was no history of stomach trouble in this case. The smooth elastic cyst had evidently not interfered with the stomach functioning or emptying.

In De Jong's fourth case, a man aged thirty-eight had suffered severely from stomach disturbances for eight years. No tumor could be palpated in the stomach and on the assumption of a duodenal ulcer the abdomen was opened. Nothing abnormal was found except a small bunch close to the pylorus, with a broad base in the mucosa. It was about the size of a pea but covered a space as large as a finger-nail. It was easily resected and the patient was freed at one stroke from all his disturbances. The tumor proved to be aberrant, but apparently normal, pancreas tissue. Illustrations are given of sections of the tumors in the various cases.

Gastroptosis. Hertz¹ rightly says: "Gastroptosis is often diagnosed without considering sufficiently whether it can be the cause of the symptoms which are present. It is, in fact, an incomplete diagnosis, as it is necessary to know whether the ptosis is present in the erect position only or also upon lying down, whether it gives rise to duodenal kinking, and, if so, to what degree stasis results, before an accurate prognosis can be given and a rational line of treatment instituted."

Orthostatic gastroptosis he describes as the condition in which the lesser curvature, after a basium meal, is below the umbilicus in the erect position, but the greater curvature is above the umbilicus in the horizontal position (Fig. 18).

¹ Arch. of Rad. and Electrotherapy, 1915, xx, 143.

velops symptoms similar to those produced by the original lesion, such symptoms being persistent and unrelieved by any medication, it is fair to assume that an ulcer has occurred in the region of the anastomosis. It is most characteristic of a gastro-jejunal ulcer if, together with symptoms resembling those produced by the first lesion, there is pain to the left of the midline and below the umbilicus. Much assistance in diagnosis may be expected from the röntgenologist, and it is this aspect of the subject that the authors have under discussion.

After gastro-enterostomy, the following conditions are found normally:

1. The opaque meal passes freely from the stoma.
2. No retention is present in the stomach from a six-hour meal.
3. The duodenum is not dilated.
4. The stomach is usually small.
5. Peristalsis is not overactive.
6. The gastric contour in the vicinity of the stoma is not deformed, except for an occasional slight dimpling at that point.
7. The efferent limit of the jejunum is neither narrowed nor markedly irregular in outline.
8. Extensive adhesions about the stoma are uncommon and the stomach is moderately mobile.
9. The stomach is not deformed, and has no tendency to hour-glass contraction or spasticity.

In nearly all cases of gastrojejunal ulcer there are definite röntgenologic indications of an abnormal condition, and there are, in many instances, more or less direct signs pointing to the location of the trouble. The most direct evidence is marked deformity about the stoma, although in other cases the opposite of the nine normal findings have been found. Carman and Balfour wisely state that a correlation of röntgenologic and clinical data is required for the correct diagnosis. A case in point occurring in my work, was a patient, who, six months after a gastro-enterostomy for gastric ulcer, began to have, as Carman and Balfour state, recurrence of symptoms similar to those produced by the initial lesion. Stool examinations failed to discover blood, the stoma was patulous and there seemed to be no reason to suspect that the anastomosis was not functioning as it should. Attention to diet and certain medical measures have successfully combated the symptoms.

Benign Proliferation of Glands in the Stomach. De Jong¹ describes in detail 4 cases in which there had been more or less serious disturbances of the stomach. In 3 the normal glands near the pylorus had proliferated, narrowing the lumen. In the fourth case there was a lump of aberrant pancreas tissue obstructing the lumen. The assumption of malignant disease had been amply justified by the disturbances, and the discovery of the absolutely normal microscopic tissue in the tumors was a

¹ Abstract Journal of American Medical Association, 1916, lxvi, 392.

great relief. One patient was a woman aged thirty-eight, and she had had stomach trouble for over two years, with much pain and emaciation. There was also a history of a period of similar trouble at eighteen. The stomach sagged and was much dilated. The lumen at the pylorus was obstructed by a ring of enlarged Brunner's glands, and complete recovery followed resection of the pylorus and gastro-enterostomy. Nothing was found to suggest an inflammatory process. In a second case the enlarged glands formed a single tumor in the duodenum. A boy aged twelve succumbed to sarcoma of the tibia but shortly before death complained of severe abdominal pain, explained by perforation of the ulcerated and enlarged glands. The third patient was a man aged twenty-eight who died from perforating ulcers, two in the stomach and two in the duodenum. One of the former had developed on an enlarged gland. In all three the proliferating gland tissue was apparently entirely normal. The condition is not like that of congenital hypertrophy of the pylorus, but its cause is fully as much of a mystery as the latter. Both are primary affections. He does not know of any similar cases on record in which the connection with gastric disturbances was ascertained during life, although Alsleben has reported some similar findings in cadavers. De Jong recently discovered a small cyst at the pylorus in the cadaver of a man aged forty-six, but there was no history of stomach trouble in this case. The smooth elastic cyst had evidently not interfered with the stomach functioning or emptying.

In De Jong's fourth case, a man aged thirty-eight had suffered severely from stomach disturbances for eight years. No tumor could be palpated in the stomach and on the assumption of a duodenal ulcer the abdomen was opened. Nothing abnormal was found except a small bunch close to the pylorus, with a broad base in the mucosa. It was about the size of a pea but covered a space as large as a finger-nail. It was easily resected and the patient was freed at one stroke from all his disturbances. The tumor proved to be aberrant, but apparently normal, pancreas tissue. Illustrations are given of sections of the tumors in the various cases.

Gastroptosis. Hertz¹ rightly says: "Gastroptosis is often diagnosed without considering sufficiently whether it can be the cause of the symptoms which are present. It is, in fact, an incomplete diagnosis, as it is necessary to know whether the ptosis is present in the erect position only or also upon lying down, whether it gives rise to duodenal kinking, and, if so, to what degree stasis results, before an accurate prognosis can be given and a rational line of treatment instituted."

Orthostatic gastroptosis he describes as the condition in which the lesser curvature, after a basium meal, is below the umbilicus in the erect position, but the greater curvature is above the umbilicus in the horizontal position (Fig. 18).

¹ Arch. of Rad. and Electrotherapy, 1915, xx, 143.

Complete gastropptosis is that condition in which the stomach is abnormally low in the erect position and the greater curvature reaches below the umbilicus in the horizontal position (Fig. 19).



FIG. 18.—Orthostatic gastropptosis. *a*, vertical; *b*, horizontal. (Hertz.)

Hertz says it is important to note whether the stomach is able to empty itself normally. If the duodenum drops with the stomach, the

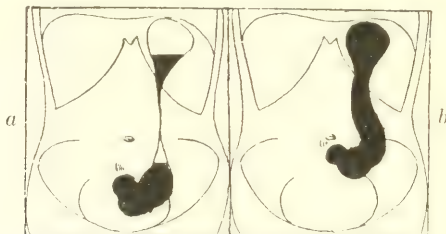


FIG. 19.—Complete gastropptosis. *a*, vertical; *b*, horizontal. (Hertz.)

emptying is usually normal. This sometimes occurs when the duodenum has not dropped but rarely in this condition, the food may pass



FIG. 20.—Complete gastropptosis with extreme stasis, especially in erect position, owing to duodenal kink. Splashing was felt in the left iliac fossa five hours after breakfast of tea and toast. *a*, vertical; *b*, horizontal. (Hertz.)

without difficulty from the stomach into the first part of the duodenum, but that there is delay beyond this point (Figs. 20 and 21).

If there is no delay in the evacuation of the stomach, indigestion is not likely to be due to the gastropotosis unless this is associated with atony, in which case the symptoms of the latter are exaggerated. Atony may be diagnosed by noting the position of the upper level of the gastric contents immediately after the opaque meal has been taken. However great the ptosis, the upper level of the contents should not be more than two inches below the highest point of the left lobe of the diaphragm. When atony is associated, Hertz terms it orthostatic hour-glass stomach (Fig. 22).

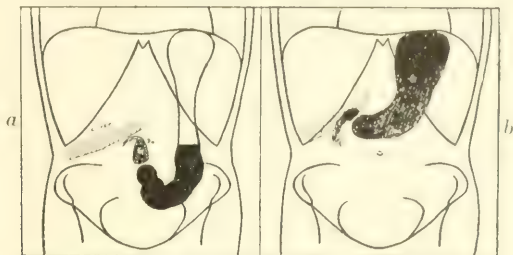


FIG. 21.—Orthostatic gastropotosis with atonic dilatation, but no stasis (empty in four hours), owing to duodenal ptosis. The liver is also seen to be dropped in the erect position. *a*, vertical; *b*, horizontal. (Hertz.)

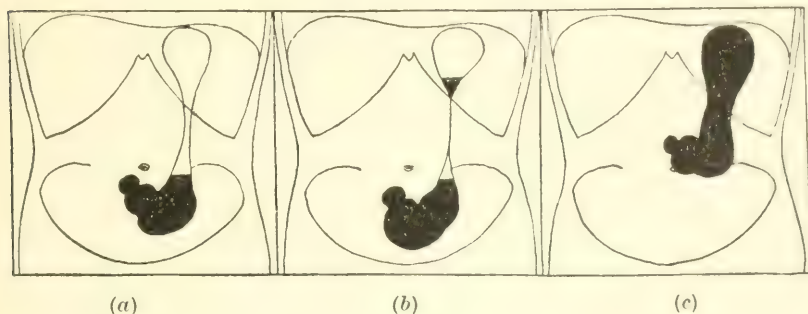


FIG. 22.—Orthostatic hour-glass stomach. (Hertz.)

This condition should never be mistaken for true hour-glass stomach, as in orthostatic hour-glass contraction the narrowing in the center of the stomach may be made to disappear if the patient contracts his abdominal muscles, or pressure is exerted on the lower part of the abdomen. If the ptosis is so extreme that the lower segment of the stomach is further depressed instead of raised by this means, it is a characteristic which serves to distinguish orthostatic and spasmodic hour-glass stomach from the organic condition.

It is interesting to read that Hertz has found how rarely an abdominal support is efficient. Hertz speaks of "ptosis of the umbilicus," *i. e.*, dropping of the umbilicus when the patient assumes the upright position. I was surprised to find how variable the umbilicus is in practically every

person. At the Polyclinic Hospital during the past winter, comparisons were made between the umbilicus and its relation to the iliac crests in the recumbent position, and this relation when the patient stood erect. Differences were very marked, even as much as 5 cm. or more in very obese individuals. Measurements made from the iliac crests are certainly more reliable, as we have in the interiliac line an unchanging landmark. Hertz recommends the use of the iliac line, but finds it is less easily seen, particularly in stout patients.

Troell's¹ study of the subject failed to show that any change in the position and movability of the stomach entails in itself alone any symptoms, or that a certain degree of such changes indicates pathological conditions. Hence he decries gastropexy for simple gastropptosis, and is strengthened in this view by the bad conditions he has encountered in some cases of the supposedly successful gastropexy. Treatment of gastropptosis disturbances should be based on all the diagnostic measures at our command, röntgenoscopy in particular. Progress will be best promoted by surveillance of the individual case, recording the effect of the various measures applied. In this borderland between medicine and surgery there is danger that the disturbances may be erroneously ascribed to neurosis. On the other hand, if an operation is done in a case of actual neurosis, the patient is liable to localize the evil at some other point.

Visceroptosis. Kantor and Levy² give a brief statistical review of material, with a view to determining the incidence of visceroptosis. Gastropptosis was decided to be present when the lowermost point of the stomach (organ filled, and patient standing) reached more than 2 to 5 cm. below a horizontal line joining the top of the iliac crests. This position was found in 57.7 per cent. of men and 72.5 per cent. of women. Under forty years of age, 69.3 per cent. had ptosis; over forty, 59.2 per cent. Of 231 men under forty, 151, or 65.3 per cent., had ptosis. Of 252 men forty years or over, 127, or 50.3 per cent., had ptosis, and of 182 women over forty years of age, 71.4 per cent. had ptosis. Childbirth had no influence on the ptotic state. Ptosis seemed to be more frequent in single women than in married women.

These figures of Levy and Kantor are interesting, but are hardly conclusive, since the patients comprising their series were all suffering from "stomach trouble." The incidence of visceroptosis in patients complaining of digestive troubles might be nearer the mark.

Relations of Splanchnoptosis to Gastric Acidity. Sandrock³ reports the result of 200 carefully studied cases of visceroptosis. He divides his cases arbitrarily into three groups according to the degree of descensus. The first-degree cases are those whose greater curvature reached to the

¹ Abstract Journal of American Medical Association, 1916, lxvi, 608.

² Boston Medical and Surgical Journal, 1916, clxxiv, 534.

³ Johns Hopkins Hospital Bull., 1915, xxvi, 262.

level of the pelvic brim; in second-degree cases the greater curvature was found below the level of the pelvic brim; in third-degree cases the stomach reached to the bottom of the pelvis. There were 25 cases of the first degree, 140 of the second degree, and 35 cases of the third degree. Marked adhesions were found in 40 cases and marked atony in 50 cases.

The average amount of stomach contents recovered increases with the degree of descensus.

First-degree amount was 41 c.c.

Second-degree amount was 56 c.c.

Third-degree amount was 72 c.c.

First-degree Ptois. The following is the result of the gastric analyses in 25 cases:

FREE HYDROCHLORIC ACID.	
Normal	40.0 per cent.
Hyperacidity	28.0 "
Subacidity	20.0 "
Achylia	12.0 "
Subacidity or achylia	32.0 "
TOTAL ACIDITY.	
Normal	32.0 per cent.
Hyperacidity	48.0 "
Subacidity	20.0 "

Sandrock accepted the usual text-book figures of normal acidity as 40 to 60 for the total and 20 to 40 for the free acid values.

Second-degree Ptois.

FREE HYDROCHLORIC ACID.	
Normal	49.2 per cent.
Hyperacidity	12.8 "
Subacidity	24.2 "
Achylia	13.5 "
Subacidity or achylia	37.7 "
TOTAL ACIDITY.	
Normal	46.4 per cent.
Hyperacidity	18.5 "
Subacidity	35.1 "

Third-degree Ptois.

FREE HYDROCHLORIC ACID.	
Normal	48.5 per cent.
Hyperacidity	25.7 "
Subacidity	17.1 "
Achylia	8.5 "
Subacidity or achylia	25.6 "
TOTAL ACIDITY.	
Normal	40.0 per cent.
Hyperacidity	34.2 "
Subacidity	25.7 "

From these tables there can be established no relation between the degree of ptosis and that of diminished acidity, the second group cases showing a much lower acidity percentage than that of either the first or third.

An average of the tables for the 200 cases of ptosis of all grades is given in the following table:

FREE HYDROCHLORIC ACID.	
Normal	48.0 per cent.
Hyperacidity	17.0 "
Subacidity	22.5 "
Achylia	12.5 "
Subacidity and achylia	35.0 "

TOTAL ACIDITY.	
Normal	43.5 per cent.
Hyperacidity	25.0 "
Subacidity	31.5 "

The free hydrochloric acid is therefore normal or diminished in 83 per cent. of all cases; the total acid, normal or diminished in 75 per cent. There seems to be, therefore, a tendency toward diminished acidity in ptotic stomachs, and hyperchlorhydria and achylia are more frequently met with than hyperchlorhydria, the ratio being 2 to 1.

Sandrock notes that the 50 cases complicated by marked atony give a still higher percentage of diminished acidity:

	FREE HCL.	TOTAL ACIDITY.
Normal	42.0 per cent.	36.0 per cent.
Hyperacidity	18.0 "	30.0 "
Subacidity or achylia	40.0 "	44.0 "

Gastritis. **TYPHOID GASTRITIS.** Plaschkes¹ has observed, in his service, many individuals who have experienced gastric discomfort following typhoid fever. These persons complained of painful pressure and fulness in the stomach after partaking of food. This discomfort lasted sometimes for hours, followed by acid or vile-tasting eructations and even vomiting. Gastric analyses were made on patients who were afebrile. The most striking feature was the presence of large amounts of mucus. The motor function seemed to be impaired also, though, unfortunately, no x-ray apparatus was available when these studies were made. In the majority of cases the total acidity, as well as the free hydrochloric acid, were below normal. Attempts were made to control or compare these results with patients suffering from paratyphus A or B, but in none of these patients was mucus present as in the typhoid cases. Plaschkes believes this form of gastritis is specific, although repeated examinations failed to reveal typhoid organisms in the gastric juice.

¹ Wien. klin. Wochenschr., 1915, xxviii, 1136.

EXFOLIATING GASTRITIS. Van Leersum¹ makes a practice of examining the stomach content and wash-water for scraps of mucosa, and has found, in the last two years, 88 such scraps, obtained from 43 patients; 9 from 1 patient. The scraps are characteristic after foliating gastritis only when found repeatedly. The pain with this operation may be considerable, but is usually less than with gastric ulcer; other symptoms may suggest gastric catarrh. A special feature of exfoliating gastritis is, that there may be intervals of weeks or months during which the stomach may be apparently normal. The other objective findings are merely tenderness in the epigastrium and some loss of flesh. Gastroscopy showed the mucosa of a somewhat different color from normal in the one case in which Van Leersum applied it, but he saw no erosions. After a test-breakfast he found, in a number of cases examined, that the acid content was never above 2.5 to 1000, and usually ranged between 0.5 and 1. He never found achylia. The stomach content is more fluid than with mucous gastritis, but when poured it threads.

Various experiments and experiences having demonstrated that the mucosa heals remarkably quickly after the scraps have been thrown off. Serious hemorrhage has never been known with it, and there is no other stomach affection which responds so readily and rapidly to treatment. This includes sparing of the stomach all irritation from insufficiently chewed and overhot food, and from spices, etc. This protects the vulnerable mucosa against injury, and it is strengthened directly by treating with an astringent. Silver nitrate is the best, and he has the patient take, three or four times daily, before meals, 15 c.c. of a solution of 0.5 gram of silver nitrate in 300 c.c. of water. A couple of bottles of this solution generally carries the patient through, but usually three or four bottles are needed, as the subsidence of symptoms does not mean that the cure is complete. This course can be repeated later if symptoms return, but the patient must be warned that this treatment should not be repeated without medical control. The nails and gums show the first signs of silver poisoning. He has noticed this even after a small or total intake of two or three grams. Discoloration of the skin occurred in one patient with a gastric ulcer who had used 6.7 grams of silver nitrate in the course of three years.

Van Leersum says all the food should be mashed soft, in purée form, unless we can convince the patient of the superior advantage of doing the soft mashing with his teeth. The habit of taking tea, coffee and soup too hot is responsible for many cases of rebellious gastritis, gingivitis, pharyngitis and chronic gastritis. When practical and convenient, instead of the above method of giving the silver nitrate, he rinses out the stomach with half a pint or more of a 1 to 4000 solution of silver nitrate, gradually doubling the strength. This can be repeated daily for

¹ Abstract Journal of American Medical Association, 1916, lxvii, 83.

two weeks, but washing with water must follow so that none of the nitrate is left in the stomach.

Lyon¹ recommends the *sectioning of gastric sediments*. The fasting stomach is aspirated for residual contents, after which it is repeatedly douched with 100 to 150 c.c. of plain warm water. The contents are filtered, the filter paper punctured and the residue is washed into a clean receptacle with a 10 per cent. formalin solution. The contents are again filtered and the tip of the filter paper containing the sediment is cut off, folded, wrapped in a layer of gauze and tied. The material thus obtained is hardened, sectioned, stained and examined microscopically.

Normally, one finds occasional epithelial cells and occasional leukocytes. There may be found crystals of some of the bile salts and the snail-like bodies supposed to be mucus. Pathologically, one may find remnants of food eaten the night before, sarcinæ and yeast cells, bits of mucosa and many other substances, which will be mentioned later.

Gastric Carcinoma. It is not uncommon to find fragments of gastric mucosa showing tubules with broken basement membranes and atypical proliferation of the epithelial cells. Oppler-Boas bacilli are found, and Lyon believes these point to cancer if the chemical analysis of the gastric juice approaches the subacid or anacid curve. Even if definitely diagnostic cancer cells or bits of mucosa showing malignancy cannot be found, the presence of areas of necrosis showing leukocytic infiltration and bacterial invasion strongly suggest ulcer or cancer.

Gastric Ulcer. What was said in the above sentence holds here, and the absence of Oppler-Boas bacilli is also suggestive. If there are bits of well-staining mucosa, the diagnosis would be much more certain. Exfoliated epithelial cells reacting well to eosin, with occult blood and a normal or hyperchlorhydric curve points to ulcer.

Chronic Gastritis. Here the diagnosis depends on the presence of fragments or flakes of mucous membrane presenting a well-marked hyperplasia of the glandular elements, with good staining power of the cells.

Atrophic Gastritis. In the recovered mucosa there is a considerable diminution in the number of the gastric tubules with well-marked irregularity in their distribution. The cells stain poorly and show mucoid and fatty degeneration with marked vacuolization. All the epithelium may be completely denuded from the tubule, leaving empty spaces in the mucosa.

Achylia Gastritis. The picture resembles that in the foregoing, together with a significant increase in connective tissue in the interglandular stoma, which Lyon suggests may be a forerunner of linitis plastica.

Gastric Atony with Dilatation. The sediment is usually negative except for amorphous debris and patches of mucus enmeshing leukocytes.

¹ American Journal of Medical Sciences, 1915, cl, 402.

Gastric Dilatation with Fermentation. In addition to the above, there will be found sarcinae, germinating yeast cells, spore-bearing fungi and mycelial threads.

Reichmann's Disease. The sediments are negative except for an amorphous débris with crystalline bile salts.

Throughout his paper, Lyon insists that the routine study of gastric sediments is of value only when taken in conjunction with critical clinical scrutiny of the case.

Gastric Mucosa in Delirium Tremens. Hirsch¹ made a study of the mucosa of the stomach in patients dying in delirium tremens, and found hemorrhages of varying size to be the rule. The largest are easily detected, but the microscope must be used for the smaller ones. The hemorrhagic areas are not found in the submucous or muscular layers of the mucosa, but are immediately adjacent to the stomach lumen. Apart from these hemorrhages, the stomach in delirium tremens is unchanged, a point of much interest, as chronic alcoholism is believed in many quarters to be productive of a chronic catarrhal gastritis.

The presence of the hemorrhagic areas has a great diagnostic value, and, when taken in connection with all other data, is almost typical of delirium tremens.

The interesting feature of Hirsch's paper to clinicians is the statement that chronic alcoholism is of doubtful etiological importance in causing chronic gastritis. This seems not in accord with the facts brought out by Vogelin and Wiltrup, an abstract of whose paper follows:

Dyspepsia and Chronic Alcoholism.² Vogelin and Wiltrup have made a special study of conditions in regard to the digestive processes in 12 hard drinkers who have been under prolonged observation, and in 45 others more recently examined. The findings after an Ewald meal, repeated from three to eight times in the course of three years, are tabulated for the first group, and also the findings with tests for secretion, motor functioning, pepsin digestion and secretion of mucus as applied more recently, in the other subjects. Gastritis and achylia are the rule, but a number of factors combine to induce them, not only the liquor but also the irregular meals and habits of life of persons addicted to alcohol. Achylia was pronounced in 50 per cent. When the patients enter the hospital and get regular food and rest, the stomach usually rapidly recuperates, and, as the gastritis subsides, the achylia subsides with it. This is similar to the experience with achylia and apparently pernicious anemia encountered with *Bothriocephalus latus*; both usually retrogress completely after expulsion of the worm. In chronic alcoholism, the recuperation proceeds most rapidly and completely in the young. Syphilis was present in a few of the cases. Nothing was found

¹ Arch. Int. Med., 1916, xvii, 354.

² Abstract Journal of American Medical Association, 1916, lxvi, 1498.

to indicate that alcoholic gastritis commences with hypersecretion. Study of all the material has shown that determination of the pepsin may be important for the prognosis, as the achylia did not retrogress in the few with pepsin. The discovery of inadequate pepsin secretion therefore prophesies permanent achylia.

Gastric Motility. The chyme, normally, does not pass through the pylorus at the approach of every peristaltic wave, but emerges occasionally at irregular intervals of from 10 to 80 seconds. Acid above, opens, and acid below closes, the pylorus. Fats, when given, are almost invariably present in the stomach during seven hours' observation. Water begins to enter the intestine almost as soon as it enters the stomach. Carbohydrates go through rapidly, proteins more slowly. When carbohydrate and proteins are given one after another, the early rate of evacuation is largely the same as that of the first food given. Mixture of carbohydrates and proteins have an emptying rate intermediate between that of carbohydrates and that of proteins. Fat retards the exit of either foodstuff from the stomach. As to consistency of food materials, there is a marked retardation of the outgo of food from the stomach when hard particles are present. Considerable amounts of gas in the stomach retard the discharge of food. Rage, distress, anxiety, grief, anger and violent emotion have a depressive effect on gastric motor activities.¹ The authors go on to say that, in addition to the physiological variations affecting gastric emptying, there are pathological alterations of exaggeration or a diminution of motility. In non-obstructive duodenal ulcer and cancer of the stomach (non-obstructive) the evacuation time is shortened, and the emptying is delayed in atony of the stomach, hyperacidity and pylorospasm from whatever cause. Marked retention, too, accompanies organic stenoses near or at the pylorus.

Carman and Miller have, in 950 cases, made comparative studies with the Riegel meal with *x*-ray examination. The latter is based on Haudek's work with the double-meal method. He gave, be it recalled, a Rieder meal in the morning, and examined the patient six hours later, at which time a second Rieder meal was given. Six hours' time was selected by Haudek as the dividing line between normal and delayed emptying, because, while a normal stomach will expel a Rieder meal in three hours, a delay of five or six hours might result from physiological causes. Carman and Miller, while endorsing Haudek's method, have modified it by giving a cereal porridge instead of a pap, and barium sulphate instead of bismuth. Since barium leaves the stomach earlier than bismuth, they believe a four-hour retention of barium is more significant than one of bismuth. Their routine is as follows:

The patient comes to the laboratory in the morning without breakfast,

¹ Carman, quoted by Carman and Miller, *Archives of Internal Medicine*, 1915, xvi, 406.

but not always, after tubing and lavage by the gastro-enterologist. He is given a meal consisting of four ounces of well-cooked wheaten breakfast cereal with 20 mm. of barium sulphate, to which he is allowed to add a little milk and sugar according to his taste. He is instructed to take neither food nor drink until the examination is finished. Six hours later he returns, and the screen examination is begun. The presence or absence of residue is noted. The amount of retention is recorded on a scale of four units, each unit corresponding to a fourth of the meal. If the entire meal has passed into the intestine, its position and distribution are noted. The patient is then given 2 ounces of barium sulphate in 8 ounces of water. Usually some of this escapes from the pylorus, showing this latter's condition as to potency. To complete the examination and to fill the stomach for röntgenography, the patient takes about 12 ounces of a potato-starch pap containing 3 ounces of barium sulphate, after which the behavior of the stomach in all respects is watched.

The gastro-enterologist's routine is the following: At 6 P.M. previous to the day of examination, he is instructed to eat an ordinary meal which must include bread, meat, and potatoes. An hour later he eats twenty raisins, the skins of which are easy to identify. The gastro-enterologist's examinations are begun the next morning at eight o'clock, the interval after the motor meal varying from 14 to 16 hours. The estimate of motility is based on the presence or absence of food bits or raisin skins from this meal, as shown by tubing at the morning examination. Residues are recorded on a scale of four.

	Ttl. No.	With residue, x-ray.		With food remnants (tube).		With residue (x-ray) only.		With food remnant (tube) only.		Number with both residue, x-ray, and food remnants (tube).		Number without residue, x-ray or food remnants (tube).		Number with resi- due, x-ray, or food remnants (tube) or both.	
		No.	p.c.	No.	p.c.	No.	p.c.	No.	p.c.	No.	p.c.	No.	p.c.	No.	p.c.
Lesion of appendix	125	1	0.8	2	1.6	1	0.8	2	1.6	0	0.0	122		3	
Lesion of gall- bladder	311	10	3.2	5	1.6	7	2.2	2	0.6	3	0.9	299		12	
Gastric ulcer	109	50	45.8	25	22.9	29	26.6	4	3.5	21	19.2	55		54	
Gastric cancer	137	83	60.5	57	41.6	29	21.1	3	2.1	54	39.4	51		86	
Duodenal ulcer	268	76	28.3	42	15.6	39	14.5	5	1.8	37	13.8	187		81	
	950	220	23.1	131	13.7	105	11.0	16	1.6	115	12.1	714		236	

FIG. 23

It will be seen from the table that there are discrepancies between the gastro-enterologist's result and the x-ray, and these discrepancies may be explained by supposing:

1. The time elapsing between the ingestion of the gastro-enterologist's meal and its withdrawal is too liberal, and that the stomach was empty in many cases, although an actual and pathological hypomotility existed.

2. It is possible that the tube may have failed to bring up food remnants which were present.

3. The tube may have failed to reach food retained in the lower loculus of an hour-glass stomach.

4. Marked differences as to the quantity and character of the food taken may have affected the gastro-enterologist's results.

5. In some cases of organic pyloric stenosis, the tube found retained raisin skins when the x-ray test failed to show a barium retention. It is clear that a stenosis might be sufficiently narrow to block the passage of these skins, yet large enough to allow of the exit of finely divided barium.

Carman and Miller believe, therefore, that the bariumized carbohydrate meal is a more sensitive test for motility than the Riegel meal. It shows not only evacuation beyond six hours, but also yields information as to hypermobile conditions, and often by showing both the active and passive factors concerned in motility, aids in the judgment of the net result. Nine times out of ten a distinct residue indicates grave obstruction at or near the pylorus.

Levy and Kantor¹ have made similar studies, using the modified Rieder meal and the modified Riegel meal. They believe that the x-ray examination should always be supplemented by the use of the stomach-tube after the administration of a motor meal, for they have observed the existence of delayed emptying in a large number of individuals who got rid of their opaque meal within the normal time limits (21 per cent.).

The chief factors influencing gastric emptying:

1. *Shape of Stomach.* As a rule, the nearer the pylorus is to the lower pole, the sooner will the stomach empty itself.

2. *Character of the Meal.* The amount, chemical nature and physical form of the food selected, each plays an important role in determining the emptying time. An opaque meal leaves the stomach sooner than a full dinner; carbohydrates leave sooner than proteins or fats, fluids sooner than solids.

3. *Form of Stomach.* Normally, the stomach "grasps" its contents firmly, and is seen to be filled to the cardia. In atony or myasthenia gastrica, the stomach is generally ptosed, the magenblase long and pyriform, the pars media is the narrowest portion of the organ, and the walls are often in contact. The stomach looks and fills like a sack. The peristalsis is usually diminished. Of 240 cases of atonic stomach, 30 per cent. failed to expel the Rieder meal in six hours, and conversely, 54.6 per cent. of the Röntgen-ray cases of delayed emptying showed atony.

4. *Acidity of Gastric Juice.* The lower the acidity, the more rapid the emptying, and the higher the acidity, the slower the emptying. In

¹ Archives of Internal Medicine, 1916, xvii, 476.

anacidity there is loss of the pyloric reflex; in hyperacidity, spasm of the pylorus. Of 154 cases of anacidity, 9 per cent. showed delay; of 748 hyperacidities, 10.4 per cent showed delay.

5. *Nervous Factors.* The nervous system may influence the gastric emptying in two ways. First, spasm due to increased acidity, or spasm due to reflex causes outside the stomach, as in diseases of the gall-bladder.

Another type of retarded propulsion occurs in fatigue, emotional states or intoxication.

6. *Mechanical obstruction.* Foreign bodies rarely cause delayed emptying. The most frequent causes are new growths or indurated ulcers at the pylorus, and mechanical factors outside the stomach in the neighborhood of the pylorus.

The immediate and actual causes of delayed gastric emptying in the order of their frequency are:

Spasm	58.8 per cent.
Obstruction	21.2 "
Atony	17.0 "
Undetermined	2.8 "

Diseases predisposing to delayed gastric emptying. The following table shows the clinical diagnosis in 185 cases of delayed motility:

Ulcer	40.5 per cent.
Diagnosis not clear	13.5 "
Unexplained high acidity	9.1 "
Auto-intoxication (including migraine)	7.5 "
Carcinoma	7.5 "
Ptois with atony	7.0 "
Cholelithiasis	3.7 "
Adhesions (intestinal)	2.7 "
Tuberculosis (systemic)	2.1 "
Chronic appendicitis	1.0 "
After gastro-enterostomy	1.0 "
Extra gastric pressure	1.0 "
Carcinoma of colon	0.5 "
Mucous colitis	0.5 "
Nephrolithiasis	0.5 "
Apprehension neurosis	0.5 "

To summarize this very good paper, the only criticism of which is, that Levy and Kantor's cases lack the operative control to be found in Carman and Miller's series, the immediate causes of delayed gastric emptying are spasm in 58.8 per cent., pyloric obstruction in 22.2 per cent., and atony of the stomach in 17 per cent. The causes of delayed emptying are in the stomach in 75.3 per cent. of the cases, elsewhere in the digestive tract in 10.3 per cent. and outside the digestive tract in 13.4 per cent. The conditions most commonly predisposing to, or associated with, delayed motility are: (*a*) ulcer, in about 50 per cent.; (*b* and *c*)

auto-intoxication and cancer, each 7.5 per cent.; (d) ptosis with atony, 7 per cent.; and (e) cholelithiasis, 3.7 per cent.

The authors are not in accord with Carman and Miller as to the value of the x-ray in testing gastric emptying, claiming that it is not delicate enough for many clinical purposes, and recommending instead the use of a meal of ordinary bulk, and determining the residue at the end of seven hours.

Experimental Partial Stenosis of the Pylorus and Motility of the Empty Stomach. By using a very ingenious technic, Elsesser¹ was able to obtain tracings showing contractions of the stomach. A partial stenosis of the pylorus induces a hypermotility in the stomach irrespective of the presence of food in the stomach. It is suggested that in individuals with a similar condition of the pylorus, there should be more persistent and vigorous stomach pangs when the stomach is empty. That this is not true, clinically, Elsesser believes is due to a change in the sensory mechanism of the stomach paralleling the motor and secretory changes.

Achylia Gastrica. Rehfuess² claims that many of the so-called cases of achylia gastrica which have been so diagnosed by the usual gastric analysis may prove to be, when the fractional method is employed, cases of psychical achylia. That is, a total absence of secretion during the first hour of digestion followed by a perceptible secretion in the second hour. A total lack of secretion during both phases indicates true achylia. An interesting observation shows the effect on total achylia of parathyroid extract. With this preparation plus local treatment, the acidity increased from a very low amount to nearly 60 at the end of an hour and a half.

Syphilis of the Stomach. That syphilis of the stomach is not so rare as was formerly believed is shown by the fact that in the past six years no fewer than 25 cases have been placed on record in the United States alone, while previously there had been but 70 authentic instances of the affection reported. Smithies³ found 26 cases in the examination of 7,545 patients suffering with all types of dyspepsia, or one instance in every 300 gastric cases (0.34 per cent.). It has been stated that gastric syphilis manifests itself abruptly in late life without any previous history of digestive disturbance, but in Smithies' series the average duration of dyspepsia was eight to four years. The cases group themselves into three divisions: (1) instances in which a persistent gastric derangement appeared in individuals who had had no previous digestive upset; (2) instances in which a constant dyspepsia followed years of antecedent intermittent dyspepsia; (3) instances in which continuous gastric upset arose in persons who had gastric disturbance at some past period, but who had been, for years, free from digestive disturbances.

¹ American Journal of Physiology, 1916, xxxix, 303

² American Journal of Medical Sciences, 1915, cl, 72.

³ Journal of American Medical Association, 1915, lxx, 572.

Laboratory Data. Hemoglobin averaged 74 per cent. Of 12 cases tested, positive reactions for occult blood in the feces were obtained in two. The average free HCl was 33, the average total acidity 51.4. Lactic acid was found in 3 cases. The Wolff-Junglaus test was positive in 5 cases. The formal index averaged 10.2, while in carcinoma the average index was 21. The x-ray revealed no pathognomonic signs. The Wassermann-Noguchi test is very important.

The most satisfactory therapeutic results are obtained by salvarsan intravenously and a thorough course of mercury and iodides.

Hayem¹ reports the case of an elderly man, who exhibited a large, immovable tumor in the epigastrium, painful, somewhat soft, and smooth. The history revealing a syphilitic infection, Hayem determined to try antisiphilitic treatment, mercury by inunction and potassium iodide by mouth. This was continued for some time without any appreciable difference being seen in the man's condition, locally or generally. Emaciation progressed, he became more feeble, but the true cachexia was missing. Benzoate of mercury was then given hypodermically, 2 centigrams every two days, and after 3 injections there was a notable change, one could no longer feel the tumor, pain disappeared, the liver remained enlarged. After twenty injections, the patient was practically well. Hayem terms his case "pseudocancer of the stomach of syphilitic origin."

Neurasthenia Gastrica. By this term, McClure² does not mean to imply that the neurasthenia associated with such symptoms is necessarily produced by a primary gastric fault, nor is he in any degree deterred from the use of the title by the consideration that the word "gastrica" will not of necessity imply gastric disturbance as a primary event, but the existence of such disturbance as part of the clinical picture. Neurasthenia is, in all probability, due to a disturbance of the normal balance of the internal secretions, which loss of balance may be the result of some overaction of one or another of the great group of ductless glands, either from an inborn tendency or as the result of some outside influence, whether nervous or toxic.

The train of symptoms associated with neurasthenia gastrica is constant. Patients complain of being easily tired, physically and mentally. They suffer from lack of concentration, and have frequent attacks of headache. There is uneasiness in the left hypochondrium and epigastrium. The gastric symptoms become at times obstructive—attacks of nausea and almost constant burning in the region of the stomach one to three hours after eating, flatulence, sense of obstruction on swallowing, salivation, constipation. Attacks of palpitation often occur, frequently without apparent cause. Cardiac pains may be present, simulating

¹ Bull. de l'Acad. de Méd., 1916, lxxv, 247.

² Lancet, 1915, ii, 695.

angina. Insomnia is characteristic, those who go to bed early have their sleep broken about 2 or 3 A.M., those who retire late are disturbed at 6 or 7. The wakefulness is induced by gastric discomfort, but many individuals have no particular distress in the region of the stomach. McClure calls attention to the Lane picture of intestinal stasis. Psychasthenia comes later. The pulse rate may be as low as 55 to 60, or may be 120 to 140. Appetite is poor, and they suffer from a sinking feeling in the epigastrium two or three hours after meals, this sensation being relieved by drinking milk or eating something. Pain may be present, and relief is obtained in the same way. In the majority of cases the gastric acidity is high, due sometimes to the hyperchlorhydria and again to organic acids. The blood pressure is low.

Physical examination discloses characteristic findings in the condition of the abdomen. Dilatation of the stomach is always present, due to spasmodic contractions of the pylorus.

Treatment follows the general lines of ordinary neurasthenia, and careful dieting must be enforced. Removal of any source of irritation or toxemia apart from the stomach is essential. The mouth should be examined and any disease remedied. The nose and throat must receive attention, likewise the appendix and the reproductive apparatus, particularly in women. These having been attended to, McClure recommends the following manipulation:

The patient lies on his back in bed or on a couch; the physician sits on his right side facing the head and places the phonendoscope over the pyloric region of the stomach. With the fingers of the right hand he strokes the skin very lightly just inside the cartilages from the 10th to the 7th rib on the left side of the patient. The stroking should be intermittent and a slight vibrating character given to the movement. The skin is stimulated in this way until a contraction of the stomach is induced, this contraction being expressed by a succession of explosive or gurgling sounds audible through the phonendoscope due to the passage of gas or fluid through the pylorus. The moment that this takes place, stimulation of the skin should be intermittent until the sounds have entirely ceased. The process is then repeated until another contraction takes place, when another pause is made until all sounds cease. Treatment in this way is carried on for twenty to thirty minutes, at the end of which time it is usually found that the size of the stomach is considerably reduced. In most cases it is advisable to continue this treatment daily for several weeks, and then gradually reduced until but one a week is given. The best time to give a treatment is some hours after a meal, at a time when the stomach is supposedly empty.

Contraction of the stomach following stimulation of the skin is in the nature of a true reflex, due to indirect stimulation of the vagus. Light touch is essential, as heavy pressure over the area indicated will not give rise to a satisfactory reflex.

Gastric Vertigo. Some authors believe vertigo is associated very frequently with hypochlorhydria, but Linossier¹ finds it more commonly in hyperchlorhydria. His observation tallies with that of most observers, I believe. The vertigo appears particularly when fasting, or at the end of the digestive period, as is common with most reflex phenomena of hyperchlorhydriacs. It is controlled by eating, or by taking alkalis, or even by drinking plain water. Vertigo of gastric origin may resemble very closely that seen in Ménière's disease, even that of agonized states such as is found in agoraphobia.

Of diagnostic help are the following points:

1. Predominance, during the vertiginous crisis, of gastric symptoms—nausea, vomiting.
2. Coincidence of vertigo with dyspeptic trouble.
3. Relation of vertigo to digestive period, provoked in some instances by certain foods.
4. Good results from treating only the gastric condition.

Of these four criteria, the first is least important, as gastric symptoms are not at all uncommon in pure Ménière's disease.

Linossier believes that in cases of vertigo of "desequilibration," occurring presumably in cases of gastric disease, if a complete examination be made of the ear and use made of the labyrinth functional tests devised by Barany, fewer cases of gastric vertigo of this type will be reported. The danger of referring all cases of vertigo to the basis of auricular disease must be avoided, and if this danger be not recognized, Linossier believes many cases will be denied treatment which would otherwise control their vertigo. He says that many cases may be vestibular as far as the mechanism is concerned, but exhibit no vertigo until the stomach provides the stimulus for the discharge of vertiginous symptoms. Without a spark there is no explosion, and without disease of the stomach there is no vertigo.

What is the mechanism by means of which the stomach provokes an attack? Trousseau ascribed it to cerebral anemia, and Bouchard to intoxication. Linossier is disposed to admit that the pneumogastric provides the centripetal path, otherwise cardiac vertigo, laryngeal vertigo, which are to be compared with gastric vertigo cannot be explained. It must be emphasized that vertigo is not an expression of trouble arising in the pneumogastric nerve, and not outside it. Excitation of itself does not cause vertigo, it but reacts on filaments of other nerves.

Instead of dividing the vertigos of disequilibration into two groups, auricular and gastric, Linossier makes three groups, auricular vertigo, gastric vertigo and auricular-gastric vertigo. He is most emphatic in urging upon the aurist the necessity of recognizing the association of

¹ Bull. de l'Acad. de Méd., 1916, lxxv, 214.

stomach and ear in all cases of Ménière's disease and he believes if attention is given the stomach, there will be more success attending the treatment of such cases.

Umbilical Dyspepsia. Aaron¹ describes dyspepsia due to a defect in the abdominal parieties. All the patients have symptoms of nervous dyspepsia due to irritation of the autonomic nervous system. They may be free of symptoms for days, and then recurrence is seen, often from the most trivial cause. The appetite is capricious, and the quality and kind of food seems to play no role in the aggravation of symptoms. Fulness of the head, headache, inability to work, vertigo, lassitude and depression are complained of. There may be uneasy sensations from one to two hours after meals, and again, heaviness is experienced immediately after eating. Constipation is the rule. Loss of weight follows, due to refusal of patient to take nourishment. Palpation of the umbilical region causes pain which is referred in different parts of the abdomen often distant from the site of pressure. Hyperacidity is present in some cases, in others gastric functioning is normal.

Treatment consists of supporting the abdominal parieties with adhesive plaster, which is continued for from eight to ten weeks, and following this, or coincident with it, an elastic abdominal support. Medical treatment is determined by the result of gastric analysis.

Myoma of the Stomach. There is, as yet, no suggestive symptom-complex of this condition, no case having been diagnosed before operation or autopsy. The clinical division into internal and external is eminently practical. The internal myoma in location and symptomatology is identical with carcinoma of the stomach and is nearly always mistaken for a malignant growth. Its long duration may be a point in differential diagnosis. The external myoma offers little prospects for diagnosis and treatment. Freely movable large tumors with long pedicles, even allowing the mass to reach the pelvis, should be susceptible to the fine points of differential diagnosis and particularly to successful operation. Despite the fact that the tumor may be actually some distance from the stomach, the dragging on that organ makes the symptoms predominantly and significantly gastric and epigastric. The mass is variously disguised as tumor or cyst of the omentum, mesentery, kidney or ovaries.²

Concrement in Stomach. Grinenko³ reports a case of a shellac concrement in the stomach as large as a man's fist. Such stones are difficult to diagnose as they may stimulate a pyloric cancer, an omental tumor, a floating kidney, or a tumor of the transverse colon. The only subjective symptom was pain in the epigastric region. The Röntgen findings differ from those usually found with cancer. The concrement consisted of

¹ Journal of American Medical Association, 1916, lxvi, 1534.

² James and Sappington, Surgery, Gynecology and Obstetrics, 1915, xxi, 744.

³ Abstract Journal of American Medical Association, 1915, lxv, 658.

shellac and was due to drinking varnish, the alcohol from the varnish was absorbed, leaving the shellac as a hard mass.

Movements of the Empty Stomach in Pathological States. Using the method employed in recording gastric contractions in dogs, Luckhardt and Hamburger¹ have studied the same problem in human subjects. Their main deductions are, that when a man experiences hunger, gastric contractions are noted. In acute gastritis, anorexia is accompanied by cessation of contractions. The polyphagia of diabetes results from vigorous contractions of the empty stomach which are responsible for the polyphagia exhibited by patients suffering with this disease.

Studies on the Normal Stomach. CHEMISTRY OF NORMAL HUMAN GASTRIC JUICE. The gastric juice was obtained by Carlson² from his well-known Mr. V., his gastric fistula case with complete cicatricial stenosis of the esophagus.

1. *Solids of the Gastric Juice.* The appetite juice contains solids varying from 0.48 to 0.58 gram per 100 c.c., of which 0.34 gr. to 0.47 gr. is organic, and 0.11 to 0.14 is inorganic material. The hunger gastric juice is distinctly higher than the appetite juice in total and in organic solids.

2. The specific gravity varies between 1.006 and 1.009 with an average of 1.007. The specific gravity of the hunger juice is higher than that of the appetite juice series since the solids are higher.

3. Osmotic concentration of the gastric juice varies; for instance, the hunger juice has, on the whole, a lower osmotic concentration than the appetite juice.

4. (I) Nitrogen averages 0.06 gram per 100 c.c. of appetite juice; the hunger juice was not examined. It is probable that some of the nitrogen is present in non-protein combinations, such as ammonia, amino acid and sulphocyanic acid.

(II) Ammonia varies from 2 to 3 mg. per 100 c.c. of juice, and appears to be slightly more concentrated in the continuous secretion or hunger juice than in the appetite juice. Carlson limits the origin of the gastric juice ammonia to the following factors:

(a) Active excretion from the blood, in which case one would expect an increase in the ammonia in increasing blood ammonia. In normal individuals there seems to be a decrease in the elimination of ammonia by the kidneys during gastric secretion.

(b) The ammonia may be found in the secretion process itself.

(c) Action of HCl on cells of the mucosa (splitting off of ammonia by the cells as a protective measure against the action of strong acids).

(d) Action of HCl on the protein of the gastric juice (conversion of alkaline and neutral proteins to acid proteins).

¹ Journal of American Medical Association, 1916, lxxi, 1831.

² American Journal of Physiology, 1915, xxxviii, 248.

(III) Amino acids. Normal human gastric juice contains slightly more amino acid than ammonia nitrogen, but the greater part of the juice nitrogen is associated with the more complex proteins.

(IV) Autodigestion. When fresh gastric juice is incubated at 38° C. the following changes take place in the proteins and in the gastric mucin:

(a) The ropy mucin and mucin floccules are dissolved.

(b) Pink color of biuret reaction is intensified.

(c) The characteristic protein precipitation at the point of neutralization is decreased.

(d) Quantity of protein precipitated by nitric acid and by heat is reduced. It is probable that this autodigestion of the gastric juice is a factor in the continuous secretion of the gastric juice.

(V) Normal human gastric juice contains a sensitizing substance for human serum, but it is practically devoid of toxic substances, both in relation to the protein of the gastric juice and to serum proteins.

5. Acidity of normal gastric juice. Of much interest is the statement that "normal human gastric juice is equal in total acidity to the maximum acidity reported by clinical observers for so-called hyperacidity in man, and there is no evidence that the gastric glands under any pathological conditions are able to or do secrete of higher than normal acidity. Moreover, the presence of gastric juice in the stomach of full acid strength leads by itself and immediately to no untoward symptom."

6. Chlorides are very constant, the minimum being 0.49 per cent. and the maximum, 0.56 per cent. chlorine.

7. Pepsin was found to be present in excess of the needs or at least far in excess of that needed in economic digestions.

FRACTIONAL METHOD OF EXAMINING GASTRIC SECRETION. As a result of Talbot's¹ study following the suggestion made by Rehfuess, he concludes that the fractional gastric analysis offers the only logical method of examination for determining the true secretory and motor state of normal and abnormal stomachs, and that it should replace the older stomach-tube method.

In each case the tube was inserted into the twelve-hour fasting stomach, the contents being removed, measured, and examined for free hydrochloric, lactic and total acidity, and for mucus, bile and food particles. The tube is removed, an Ewald meal given and the tube immediately reintroduced. At fifteen-minute intervals, 5 c.c. specimens are removed until the contents seem free of food particles and until the free and total acidities had returned to what was found in the fasting stomach.

In a series of normal cases, the highest total acidity was 40, the lowest was 5, with an average of 17. The highest free hydrochloric

¹ Journal of American Medical Association, 1916, lxvi, 1849.

acid was 30, while 62.5, the residuum, contained no acid, giving an average of 6.37 acid for the series. The greatest amount removed was 210 c.c., the smallest 5 c.c. A study of the normal charts shows a drop in the free total acidity at the first fifteen minutes, due to dilution of appetite secretion by the Ewald meal. Talbot remarked the absence of appetite secretion in response to the Ewald meal in many cases, and this varying effect of the Ewald meal on the appetite secretion must be borne in mind. The high point in secretion occurred uniformly between the one hour and fifteen minute, and one hour and forty-five minute periods. In no instance was it encountered in one hour, the conventional time for removing the Ewald meal. The high point of secretion varied from forty-five minutes to two hours, fifteen minutes after the test-meal was taken.

It is important to realize from Talbot's work, as well as from that of Rehfuess, that there is no form of secretory curve which is common to all normal stomachs, nor is there a chemical curve which is uniform, although it is probable that the gastric juice, as it flows from the glands, possesses a constant acidity (Pawlow, Calson).

RETENTION TUBE IN STUDY OF GASTRIC CHEMISTRY. Lanza¹ expatiates on the important information that can be obtained by examining the stomach content every ten to fifteen minutes after a test-meal, leaving the stomach-tube in place for several hours. A very fine tube is used for the purpose and it is not introduced until after the meal, so it does not in itself stimulate the stomach to extra secretion or peristalsis. Comparative tests with other technics confirmed the indifference of the stomach to this method, and demonstrated its reliability. Fifteen charts are given to show the curves representing gastric functioning in persons with normal stomachs or with various affections involving the stomach more or less directly. The findings are obviously far more instructive than when the stomach content is examined only once after an arbitrary interval. In chlorosis he detected, by the technic, tardy hyperacidity which would have escaped ordinary methods of examination. He never left the tube in place for more than two hours at a time.

ACIDITY OF UNDILUTED GASTRIC JUICE. Menten² made studies of the acidity, using Michaelis's method of estimating the hydrogen-ion content. Of great interest to clinicians and to those who depend upon titration for the determination of acidity is the statement of Menten to the effect that the results obtained were in very good agreement with those obtained by Carlson (q. v.) in the same specimens by titration.

MECHANISM OF NEUTRALIZING THE ACIDITY IN STOMACH AND INTESTINE. Zaitzeff³ studied the mechanism of neutralizing the

¹ Abstract Journal of American Medical Association, 1915, lxx, 208.

² Journal Biol. Chem., 1915, xxii, 341.

³ Abstract Journal of American Medical Association, 1915, lxx, 1496.

gastric and intestinal contents on five dogs with gastric, duodenal or intestinal fistulas. Although 28 experiments were made, of which 4 were done on a dog with a pyloric fistula, he found that the neutralization of the acidity in the stomach is done by the pancreatic juice, which is also responsible for the neutralization of the acidity in the upper portion of the small intestine, and does not reach the end of the latter. The source of chlorine in the stomach is the pancreatic juice, as the proportion of chlorine increases when acids not containing chlorine, such as acetic, sulphuric, and lactic acids, are introduced into the stomach. The less concentrated the acid introduced into the stomach, the lower becomes its acidity. In the pyloric portion of the stomach, the acidity is lower than in the fundus, because of the presence of the pyloric alkaline juice. After introduction into the stomach of acid fluids, the stomach content acquires the properties of trypsin digestion, that is, proteins are digested in an alkaline medium. This also shows that pancreatic juice gets into the stomach under such circumstances.

EFFECT OF BILE ON GASTRIC ACIDITY. Grey¹ diverted the bile from the duodenum into the stomach, and followed the course of secretion of the gastric juice and the acidity of the gastric contents. These studies indicate that bile, when present in the stomach throughout the course of digestion, has no appreciable effect on the acidity of the gastric contents.

SHALL GASTRIC ACIDITY BE ESTIMATED IN FILTERED OR IN UNFILTERED GASTRIC CONTENTS? The reason why the filtrate has been selected for this purpose, according to Seidl,² is because, when gastric chemistry began to be studied, it was considered essential to carry out all tests as rigorously as one should if he were dealing with a purely chemical problem. The question whether the hydrochloric acid was equally distributed in the liquid and in the solid portions of the extractions was scarcely considered. Later, it was found that there was an appreciable difference in the two, usually a higher figure being obtained when unfiltered portions were used. Martius and Lüttke claimed that the difference in acidity was marked, and said it was not inconsequential whether filtered or unfiltered contents were employed. Whether digestion was in an advanced or in an early stage, depended the unequal or equal distribution of acid in solid or in liquid portions of the gastric contents. This all proved, according to Martius and Lüttke, that the determination of acidity in the filtrate led to false conclusions, and nothing but the contents as removed from the stomach should be examined.

Later authors have approved of this dictum, but more recently the question has been raised as to whether an exact chemical titration can

¹ Jour. Exper. Med., 1916, xxiii, 15.

² Arch. f. Verdauungskr., 1916, xxi, 196

be carried out in such a conglomerate mass as the ordinary gastric contents? Christiansen, after studying the ion concentration of the gastric juice, stated that it made very little material difference whether filtrate or pure contents were used. Seidl has again opened the question; 100 cases were studied and these were divided into two groups of 50 each. The first group of contents was thoroughly stirred, a portion examined and the remainder filtered. The second group was examined, filtered and unfiltered, without any previous stirring. Almost without exception the acidity was higher in the unfiltered contents, although the differences were not very great, rarely more than 10.

The question arose as to whether the unfiltered contents did not combine with the alkali on account of substances contained in the bread? Seidl says this is not exactly true, but the fact that unfiltered contents are more acid is due to the mechanical combining of the acid in the bread. As a result of his work, Seidl advocates that titration be carried on in unfiltered contents, first thoroughly stirring the mixture, then allowing the extractum to settle, and examining the precipitate after pouring off the supernatant liquid. The only exception he makes is when there is much mucus, in these cases filtrate must be used.

Weinberg,¹ working in Martius's laboratory, rejects the technic of Seidl, saying, if one desires to determine the acidity of the gastric contents, he must not take that portion which contains the highest acidity values (residue after standing) or the lowest (supernatant liquid) but he must use the thoroughly mixed contents, not allowing it to settle in a conical glass. Or, better still, he thinks acidity should be determined in both the filtrate and in the contents as removed from the stomach.

TEST FOR GASTRIC ACIDITY WITHOUT THE STOMACH-TUBE. Galmozzi² uses a strip of gauze about 4 or 5 cm. long by 1 cm. wide dipped in 0.5 per cent. solution of Congo red, and another similar strip in 0.5 per cent. solution of dimethylamidoazobenzol. A long thread is fastened to the two strips and both of the strips are squeezed into a capsule which the patient swallows after a test-meal. When the capsule has dissolved, the strips of gauze are withdrawn and the tint of the gauze strips indicates conditions as to the acid in the stomach content. These stomach tubeless methods emerge from the literature like a moth from its cocoon, flit into obscurity and perish. Their value is slight. Galmozzi says, "when the capsule has dissolved." What means has he for determining this? Must the string be withdrawn and the capsule inspected? The stomach-tube properly inserted is of such little discomfort that substitutes, such as have been suggested, seem

¹ Arch. f. Verdauungskr., 1916, xxi, p. 315.

² Abstract Journal of American Medical Association, 1915, lxx, 1860.

scarcely as valuable as is the paper which carries the message of its discovery.

PAPER TEST FOR FREE HYDROCHLORIC ACID. My predecessor in this department of PROGRESSIVE MEDICINE, in 1911, described the paper test or capillary analysis of gastric acidity as follows: The test is based upon the fact that when a watery solution of hydrochloric acid is placed upon filter paper, the water spreads out over a larger area than does the hydrochloric acid. Holmgren, who described the test, had prepared appropriate filter paper soaked in Congo solution. By this means the radius of the circles made by the water and the hydrochloric acid when a drop is placed on the paper may be read. By using a formula, the percentage of free hydrochloric acid may be estimated. Holmgren found this method gives higher values for hydrochloric acid than does titration using dimethylamidoazobenzol as an indicator, but that there is no definite relationship between the results obtained by the two methods. Lavenson adds that if Holmgren's test gives higher values than does titration with dimethylamidoazobenzol, it is probably of little value since the study of gastric acidity by the O-ion concentration showed that dimethylamidoazobenzol and Congo paper gave values that were much too high.

Orell¹ has been giving Holmgren's test a thorough trial, comparing it with other tests. He found that there was quite a difference between the results he obtained, and those recorded by Holmgren, and finally traces this error to the drying out of the blotting paper that had been used. It was so old that it had lost much of its absorbing properties, and the figures obtained were too high. The findings after five minutes were taken as the standard. When ten minutes had elapsed, the probability of error is enhanced.

GASTRIC RESIDUUM IN NORMAL INDIVIDUALS. Fowler, Rehfuess and Hawk² have made a study of the residuum in normal persons (100), examining for total and free acid, pepsin, trypsin, cryoscopic index and specific gravity. The authors have found an appreciable residuum always present in the stomach, averaging in all of the cases 52 to 14 c.c. In 43 per cent. of the cases the residuum was colorless and 56 per cent. yellow or green, the two forms occurring sometimes in the same individual. In some instances a negative bile reaction was obtained despite the yellow or green coloration, due probably to the spheroidal yeast cells, *Cryptococcus Salmoneus* (Sartory). Many of the residua give a positive bile reaction, and this reaction was more constant in acidities above 30 and still more so in those above 50. It is interesting to note that in the normal fasting stomach, this highly acid residuum is found and that normally there takes place this regurgitation of duo-

¹ Abstract Journal of American Medical Association, 1916, lxvi, 39.

² Journal of American Medical Association, 1915, lxx, 1021.

denal juice for the purpose of neutralization. The origin of the residuum can be explained only on the basis of a constant secretory activity of the gastric glands, and the authors have found in all of their observations a definite secretion in the stomach at all times.

Free acid is rarely met with until the total acidity is above 10. In cases of over 13.5, there were no cases in which free acid was not present. In only one instance was the total acidity over 70, a fact to be remembered when increased quantities of residuum are obtained possessing high acidity.

Pepsin was constantly found, and there seemed to be a definite relationship between the quantity of pepsin and the total acidity, when the acid values were low. When the values become higher, no proportion is apparent.

Trypsin was constantly found, another evidence of regurgitation of the duodenal contents. The ratio between trypsin and total acidity is not constant, but the ratio between free acidity and trypsin is an inverse one. The authors says, "This we can explain by the supposition that high acidities encourage closure of the pylorus, and lower acidities are accompanied, as stated above, by a certain degree of relaxation and regurgitation of pancreatic juice." This statement seems hardly consistent with the authors' remarks concerning the presence of bile, where it was assumed that the function of the duodenal contents was to neutralize the high acidities. It is difficult to see how this is possible if the pylorus is encouraged to close by high acidities. Fowler, Rehfuess and Hawk bring forward a second and more plausible supposition, to my mind, namely, that "low trypsin in high acidities may be also explained by the destruction of trypsin in high acidities." It is claimed by the writers that it is the free acidity of the gastric content which regulates the closure of the pylorus rather than the total acidity.

Cryoscopic examination showed that the index was -0.470 , which is lower than that of the blood (-0.560). The index is independent of the total acidity.

The specific gravity is inversely proportional to the total acidity. If the cryoscopic index remains the same, then in higher acidities the lighter hydrochloric acid molecules must replace other and heavier molecules. If the cryoscopic index is to remain the same, the total number of dissolved particles (ions and molecules) must remain the same. The gastric residuum is the lightest fluid of the body.

PEPSIN AND TRYPSIN. Dörner¹ has made studies on the trypsin and content of the fasting stomach. The stomach is mildly aspirated in the morning, a light dinner having been partaken of the evening before, and the pepsin estimated by the edestin method and the trypsin by the casein method. The author found it unnecessary to administer an oil meal in

¹ Deutsches Arch. f. klin. Med., 1915, cxvii, 540.

order to obtain pancreatic ferment, since with simple aspiration he has obtained trypsin in a large percentage of his cases. The cases are divided into three classes according to the acidity of the gastric contents.

In the first table he arranges his cases of large amounts of hydrochloric acid; of the 26 cases in this group only 4 had trypsin. This comprises the general experience that trypsin is destroyed in an acid medium, and it would seem, therefore, a loss of time to examine for this ferment in highly acid gastric contents. Suggestions as to neutralization of the contents *in vivo* or immediately *in vitro* are made, but they seem to have been found of little value.

The second group of cases comprises those of deficient amounts of hydrochloric acid. In this type of case trypsin was found in 83.3 per cent. of 54 cases.

In the third group of neutral or alkaline juice (30 cases) trypsin was found in 80 per cent. and pepsin in but 53 per cent.

Dorner makes the surmise that the pancreas has a continuous secretion exactly like the bile and salivary glands, and also the stomach, although the latter is not mentioned by Dorner. If, by his method of aspiration, pancreatic secretion cannot be found, then the duodenal pump or bucket must be used, but he found his technic just as efficient as the oil or cream test-meals.

NATURE OF PEPSIN. In examining commercial pepsins of varying proteolytic activity, Aldrich¹ has found a gradual decrease in the percentage of alpha amino-nitrogen in the samples in the order of their strength. He believes that in the purification of the pepsins the simple amino-nitrogen compounds are eliminated, and there is consequently an accumulation of more complex bodies in the stronger pepsins. Assuming that with the still higher pepsin, the alpha amino-nitrogen content will be still further decreased, one would finally, by sufficient purification, obtain a pepsin having very little amino-nitrogen or an amount approximating that in the native pepsin, from which Aldrich infers that the pepsins are of a more complex structure than the simpler amino-nitrogen compounds; in other words, they approach the native proteins in complexity. Aldrich, from his analyses, compares the higher pepsins with deuterio-albumose. The pepsins may therefore have been either mixtures of native proteins and their hydrochloric products, or may have consisted entirely of such products of partial hydrolysis as the lower albumoses. The total nitrogen in the samples showed very little variation.

GASTRIN. In 1906 it was shown by Edkins and by Gross that a 0.4 per cent. hydrochloric acid extract of the cardiac or pyloric mucous membrane from a hog's stomach causes a secretion of gastric juice when injected intravenously, but that similar extracts from the fundus

¹ Journal Biol. Chem., 1915, xxiii, 339.

portion are inert. It was suggested that a gastric hormone may be involved in gastric secretion.

Keeton and Koch¹ have undertaken similar studies which prove that there is certainly a definite specific substance known as gastrin. Well-washed fresh material was hashed and mixed with five times its weight of 0.4 per cent. hydrochloric acid, then heated to 90° C. on the steam bath, set aside at room temperature, the next day heated to 90° C., and, after cooling and standing for twenty-four hours, filtered. The noted volume of filtrate was then concentrated under diminished pressure to one-eighth or one-tenth its original volume. Six volumes redistilled 95 per cent. alcohol were added, allowed to stand for from one to three days, filtered, and the filtrate evaporated to dryness under diminished pressure. After dehydrating the residue by evaporating three times with 25 to 75 c.c. portions of absolute alcohol, the material was extracted three or four times with boiling absolute alcohol. The residue, insoluble in absolute alcohol, was dissolved in water, and again evaporated to dryness under pressure. This was repeated two or three times to remove the alcohol. Finally, the residue was dissolved in water, filtered, and diluted, so that 1 c.c. represented approximately 4 or 5 grams of fresh tissue. This solution was then sterilized three or four times in sealed tubes on successive days. Hog tissues were used throughout. Details of method of injection and analytical methods are given.

After injection of gastrin there is a latent period of ten to fifteen minutes; the maximum amount is secreted in the second fifteen-minute period, and the greatest acidity is found in the third quarter. Acidity and quantity go hand in hand. Pepsin is variable in amount, but seems to be increased always by an injection of gastrin. Two means of obtaining gastric juice were employed: by a fistula and by the Pawlow stomach, but, inasmuch as in the latter method no contamination by saliva, bile and intestinal contents takes place, the authors adopted this technic as the standard.

Studies were made in the distribution of gastrin in the tissues, and the following tissues were used: Mucosa from the pyloric fundus and cardiac regions, the duodenal and esophageal mucosa, pancreas, submaxillary gland, striated and smooth muscle, and brain tissue. Only the mucosa from the stomach and the duodenum gave positive gastrin reaction, the other tissues apparently containing no appreciable amount of gastrin.

When gastrin is injected, there is a lowering of blood-pressure, giving rise to the contention of Popielski that all of the effects of similar injections were due to vasodilatation. Attempts to remove "vasodilators" by extraction with hot absolute alcohol were unsuccessful, but that vasodilatation is not the cause of the secretion is shown by lowering of blood-pressure for only four or five minutes, while maximum secretion is attained thirty minutes after injection. Keeton and Koch

¹ American Journal of Physiology, 1915, xxxvii, 480.

believe that gastrin is a specific substance of a different chemical nature from pancreatic secretion, and that it causes a secretion of gastric juice which is a true secretion rather than a simple vasodilator response.

POSITION OF THE NORMAL STOMACH. "In males, when standing, the average portion of the lower border of the stomach was found to be one inch below the umbilicus, the extremes being from one inch above to three inches below this plane. In females, when standing, the lower border of the stomach was found to be three inches below the umbilical plane, the extreme being one and three-eighths to four and a half inches below. When standing, the stomach is either U- or cow-horn shaped. The pyloric valve points upward, backward and to the right. When lying down the pyloric valve is one-third of an inch below the transpyloric plane, and in 12.5 per cent. of cases it points upward, backward, and to the left; the descending portion of the duodenum then lies posterior to the pyloric portion of the stomach.

"The cardiac stomach is not a storehouse for food, as commonly stated, but, when standing, a gas pocket. The stomach fills from above downward, the upper border of its contents remaining, during filling, at the level of the esophageal opening.

"The stomach is always as big as its contents. Its shape depends upon the quantity of its contents, the position of the body, the distention of the adjacent viscera, peristalsis and respiration. In certain cases even the beat of the heart gives a blow to the stomach wall which causes a wave to run across the surface of its contents.

"The stomach is normally in a state of tonic contraction so that when one lies down, the portion of the stomach over the vertebral column tends to empty and contract while the fundic portion accommodates an increased portion of the stomach contents.

"In the erect position the fundic portion of the stomach looks upward, not backward, as stated by Hiss and Cunningham. The surfaces are not up and down, but anterior, posterior, or anterosuperior and postero-inferior as we stand or lie down. The greater curvature is not higher, but lower, than the lesser. The lesser curvature does not become convex when the stomach is filled, filling being accommodated by distention of the greater curvature. The position of the incisura angularis, with reference to the pyloric valve, varies with the high or low position of the pyloric valve.

"The normal position of the diaphragm is higher when one is in the horizontal than when in the erect position. Not infrequently contraction of the abdominal wall is accompanied by descent of the diaphragm. Though some females employ costal respiration almost entirely, as do some men, others show as great a swing of the diaphragm in normal respiration and as great extremes of movement of diaphragm in forced inspiration and expiration as is found in men."¹

¹ Myers, *Journal Indiana State Medical Association*, 1915, viii, 460.

ABDOMINAL DISEASE.

Arteriosclerosis of the Abdominal Vessels. Hedlund¹ comments on the rarity of arteriosclerosis affecting the abdominal vessels. When it occurs, it is liable to induce symptoms suggesting angina pectoris, gastric trouble or attacks of meteorism. In a case he describes in detail, the syndrome induced was that of fatal ileus. The patient was a workingman of sixty-one years, who, for two years, had complained of stomach trouble. Then came two attacks of severe colic within five days, followed in two days by the ileus. At operation, the next day, over four feet of the ileus was resected. The man did not rally, and necropsy revealed advanced arteriosclerosis almost exclusively affecting the walls of the lower part of the large intestine. There was calcification at some points. Some vessels were entirely obliterated, but no mechanical obstruction of the bowel was found at any point. Differentiation is difficult, the symptoms may be dependent on spasmodic contraction of the arteries affected, or of the part of the bowel wall involved, or they may be arteriosclerotic neuralgia. Treatment can be only symptomatic.

Abdominal Fremitus as a Sign of Chronic Peritonitis. Schchetkin² found abdominal fremitus in the right iliac region in patients suffering with chronic appendicitis, peritonitis with adhesions. This may be diagnosed clinically from the presence of this fremitus. The patient is asked to answer some questions, and while he is talking, the examiner's hand applied to the right iliac region experiences a manifest thrill or fremitus. He did not find this fremitus in acute peritonitis or in any other abdominal affection, such as dropsy, but only in chronic peritonitis accompanied by solid connective-tissue adhesions, which transmit the fremitus of the diaphragm to the right iliac region.

Chylous Ascites. A case of chylous ascites due to gastric carcinoma is reported by Outland and Clendening³ and one due to lymphosarcoma in which chylothorax was also present is published by Tuley and Graves.⁴

DISEASES OF THE INTESTINE.

Duodenal Ulcer. Boas⁵ insists that the outcome of gastro-enterostomy for duodenal ulcer is not always the success generally credited to it. Re-examination months later will often reveal the presence of occult blood. This is an objective sign that normal conditions have not been restored. Only when the gastro-enterostomy banishes the occult hemorrhages so that tests for it, months and years later, are persistently

¹ Journal of American Medical Association, 1915, lxy, 290, abstract.

² Ibid., p. 1316.

³ Ibid., 1916, lxi, 1833.

⁴ Ibid., p. 1811.

⁵ Ibid., p. 845.

negative, can we speak of an actual permanent cure. It would strengthen the stand-point of those surgeons who regard gastro-enterostomy as a sure cure for duodenal ulcer if such testimony could be adduced, but Boas's experience is against it. His view is, that gastro-enterostomy merely provides conditions which facilitate the success of a course of treatment for the ulcer. Operative treatment for recurring and intractable duodenal ulcer may be necessary, but to advocate it for every case is going too far, he thinks, unless we can present evidence that occult hemorrhage is permanently arrested by it.

NEW SYMPTOM OF DUODENAL ULCER. Stern¹ describes a posture which patients voluntarily or involuntarily assume in order to obtain relief. The patient often prefers standing to sitting, but, when sitting, he chooses a slanting position, so that chest, abdomen and legs form a perfect incline. If in bed, the patient assumes left-sided decubitus, but never lies on the right side. Stern continues by saying, "It seems almost as if the patient with duodenal ulcer occupied by preference the posture which is the reverse of that by which he has acquired the lesion. With very few exceptions, the body of an individual during the process of development of a duodenal ulcer, especially when at work, is bent over, the curve being in the pyloro-epigastric region. Very often this region infringes upon a hard object, as a working table, for instance. This is especially the case in a right-handed person. (I have never seen a case of duodenal ulcer in a left-handed person)." Stern says the sign is not present in gastric ulcer.

DIFFERENTIAL DIAGNOSIS OF DUODENAL ULCER. Wulff² compares the clinical history with the operative findings in 18 cases of pyloric ulcer, 39 of duodenal and 61 of gastric ulcer. A pyloric ulcer, or one near the pylorus or above it, was found in many cases to present the typical Bucquoy-Moynihan set of symptoms. Neither is the Hartman-Souppault pyloric syndrome restricted to cases with the ulcer at the pylorus; it may be lower down or higher up.

Van Amstel, writing with Wulff, discusses recent literature on duodenal ulcer, and describes a case of gall-stones, with no tendency to gastro-intestinal ulceration, in which the man suffered from distressing hunger-pains at night, relieved at once by eating zwieback. When symptoms attract attention to the ulcer, it is then usually in a comparatively advanced stage. The symptoms ascribed to a duodenal ulcer may be those merely of acid dyspepsia. He cites various data which emphasize that the anamnesis is rarely sufficient basis for positive diagnosis of duodenal ulcer, and normal Röntgen findings do not exclude the possibility. The ulcer is more liable to be in the duodenum than in the stomach with negative Röntgen findings. He agrees

¹ Archives of Diagnosis, 1915, viii, 360.

² Abstract Journal of American Medical Association, 1916, lxvi, 847.

with Rovsing that the diagnosis has been made erroneously in many cases, and gastro-enterostomy performed on a mere guess. Van Amstel lauds the method of introducing an electric light directly into the stomach through a minute incision when the abdomen has been opened. By this means the stomach can be inspected throughout and also the duodenum.

In conclusion, Van Amstel cites a number of cases of duodenal ulcer in young children. In a boy and girl aged fifteen and fourteen years, the operation was performed twenty-six and seventeen hours after perforation of the ulcer; recovery followed. It is possible that in some cases in which stenosis of the pylorus was assumed, the trouble may really have been duodenal ulcer. In Collin's compilation of 270 cases of duodenal ulcer, 42 were in children under ten years. Gastric ulcer is rare in children. One infant a month old succumbed to hemorrhage from a duodenal ulcer, but syphilis was incriminated in this case.

PERFORATION OF GASTRIC AND DUODENAL ULCERS. Of 40 cases operated upon by Warren,¹ 29 were men, 11 women, with a mortality of 35 per cent. The mortality of gastric ulcer was 54 per cent., while that of duodenal ulcer was about 25 per cent. The age of these patients is shown in the following table:

Age in decades.	Gastric ulcer.		Duodenal ulcer.	
	Lived.	Died.	Lived.	Died.
15 to 25	3	1	2	0
25 to 35	1	2	5	4
35 to 45	1	2	5	0
45 to 55	1	2	5	3
55 to 65	0	0	2	0

The onset of symptoms following perforation is sudden; vomiting is not a striking feature, although it occurs in most cases at some period of the attack, usually the commencement. When severe and continuous, it is a sign of grave omen. Rigidity is the cardinal sign.

The prognosis can be based on the pulse rate for one thing; when over 120 it is a serious portent.

Pulse rate.	Number of patients who lived.	Died.
70 to 90	9	4
90 to 120	10	3
120 to 150	2	6

The mortality bears a pretty definite relation to the time that elapses between perforation and operation. After twelve hours the prognosis is grave. I miss, in the author's paper, mention of the previous medical history of these patients. Some of the cases of duodenal ulcer, despite rigid cross-examination, persist in stating that previous to this sudden

¹ *Lancet*, 1915, ii, 1239.

attack of pain they have never had any symptoms of indigestion and have never had any abdominal distress. Gastric ulcer cases, generally, give histories pointing to the possibility of ulcer recently or some time previous to the perforation. This inability to obtain a history of indigestion in the duodenal cases has been of great disadvantage in diagnosing the case correctly, and I have been chagrined, when the diagnosis of acute appendicitis, made with some assurance, was later discredited by the finding of a perforated duodenal ulcer. Vomiting has occurred earlier in perforated gastric ulcer than in perforated duodenal ulcer in the cases I have seen, and the patient is more shocked in the former than in the latter instance.

STUDIES ON HYPERACIDITY AND THEIR BEARING ON DIAGNOSIS OF DUODENAL ULCER. In PROGRESSIVE MEDICINE, 1912, page 29, I devoted considerable space to the discussion of a new test-meal devised by Mintz, which had for its main object the stimulation of the appetite and the "appetitsaft." Mintz, it will be recalled, selected Liebig's beef extract for his test-meal which has a uniform composition, is homogeneous, contains little albumin and stimulates *ad maximum* the glandular activity of the stomach. From analysis the meat extract consists of

Water	17.70	per cent.
Organic substances	61.04	"
Total nitrogen	9.17	"
Insoluble and coagulable nitrogen	0.36	"
Albumose	6.01	"
Ammonia	0.59	"
Other nitrogen compounds	54.68	"

He makes a stock solution by mixing 100 grams of the beef extract with 500 c.c. of boiling water. This is filtered and sterilized. The concentration of the bouillon is measured according to the degree of acidity, 5 c.c. mixed with 100 c.c. of water has an acidity of 16 to 18. Before using it, it is mixed with 475 c.c. of warm water and 2 grams of sodium chloride, of which amount the patient drinks, 450 c.c. leaving 25 c.c. as a control.

With this meal Mintz made the interesting discovery that the stomach preserves automatically a certain acidity, and that when the acidity begins to exceed a stated degree, means of controlling it are called into play, notably the bile, whose function it is to neutralize the excessive acidity. The presence of bile is not accidental, as it occurs only when the acidity becomes excessive.

The following year, 1913, in PROGRESSIVE MEDICINE, page 18, an article by Hartiegan and Döri was abstracted. In this paper the authors reported comparative studies with the Ewald and Mintz meals, concluding that the data do not warrant one in abandoning the Ewald meal, as, for all practical purposes, the results are the same. A table published at this time shows this, and is reproduced here.

Diagnosis.	No. of cases.	No. of estimations.	Ewald.				Mintz.			
			Total acid.	Average.	Free acid.	Average.	Total acid.	Average.	Free acid.	Average.
Normal	21	25	35-62	47	19-30	24	44-84	70	19-65	44
Hyperacidity	32	53	50-90	72	32-72	51	60-99	75	30-75	53
Hypoacidity	4	4	28-43	36	0-10	10	23-52	38	9-32	19
Achlorhydria	4	6	5-22	9	13-30	23
Carcinoma	5	5	3-60	17	13-33	23

FIG. 24

In a more recent article Mintz¹ has continued his researches and has found his meal of importance in diagnosing duodenal ulcer. He has demonstrated that the absolute acidity of the gastric juice begins to increase above 50 per cent. of the entire volume of gastric contents. The absolute acidity drops to 3.7 per thousand and below; at the same time the relative acidity of the stomach content tends to retain its *status quo*. If such a decline of the acidity did not result, it is clear that with the reduction of the amount of the bouillon which is all the time flowing out into the duodenum, the acidity of the stomach content would have to increase progressively and would finally reach abnormally high amounts because the gastric juice, on the one hand, is constantly passing out with the bouillon into the intestines, and, on the other hand, more is continuously pouring out of the glands. Even when the food remains in the stomach, the so-called secretion from secretagogues in the food occurs.

With derangement of this mechanism for self-regulation of the acidity of the stomach content, the curve of the acidity of the stomach content may rise, and may reach a very high figure. He regards such cases as of great clinical interest because this irregularity of secretion was found constantly in his cases of duodenal ulcer. His conclusions from his total series of cases are: (1) That the test-bouillon shows that the excessive acidity of the stomach content depends exclusively on the so-called leveling property of the stomach. (2) Because of this self-adjusting mechanism, this digestive hypersecretion does not usually show the increased acidity of the stomach content. (3) With the Ewald test-meal, the increased acidity may be due to the derangement of the leveling faculty as well as to increase in the gastric secretion, or exaggeration of the motor functioning of the stomach, or both; in regard to the last two factors, the acidity is due not so much to the chemistry of the stomach, as to the peculiarities of the test-meal, especially the fact that it has such an insignificant stimulating action on the secretion of gastric juice. (4) Knowledge of the leveling property of the stomach easily explains

¹ Abstract Journal of American Medical Association, 1915, lxx, 1067.

numerous chemical facts which contradict the prevailing theories as to the hyperacidity of the gastric juice, and that its composition is unchangeable. The leveling faculty of the stomach may thus explain the comparatively low acidity of the pure stomach juice taken from patients with constant hypersecretion.

THE CHEMISM OF THE STOMACH WITH DUODENAL ULCER. Mintz¹ summarizes the conclusions from his chemical experiences and research as follows: (1) Hyperacidity, namely, disturbance in the "leveling" property of the stomach is a constant phenomenon in duodenal ulcer. By "leveling" property he means the remarkable faculty possessed by the normal stomach of keeping the absolute acidity at the same level. (2) The tardy pain is explained by the facts that in beginning of digestion, the gastric chemical function is normal. Several hours after the intake of food, when the large portion of gastric content has left the stomach, the leveling properties are disturbed, and gastric acidity begins to rise, causing spasm of the pylorus and attacks of pain. (3) The pain-soothing effects of food intake in duodenal ulcer can be explained by the lessened acidity of the stomach, the hydrochloric acid being combined with the food. (4) The pain-soothing action of alkalies is due to the neutralization of the excess of hydrochloric acid. The similar action from hydrochloric acid depends on its stimulation of the leveling activity of the stomach, that is, of the mechanism for self-regulation of acid secretion. (5) The six-hour bismuth residue with duodenal ulcer is due to the reflex pyloric spasm. (6) The excessive peristalsis of the stomach and its increased motor activity can be explained by the fact that the duodenal mucosa is flushed at the end of the gastric digestion by the over-acid stomach content. With gastric ulcer normal or subnormal acidity of the stomach content has been the rule in his experience. Hypersecretion was most pronounced with ulcer near the pylorus.

Duodenal Content. Lichtendorff² studied the duodenal juice by means of Einhorn's duodenal tube and bucket. He used the tube dry on an empty stomach. The color of the duodenal juice is light, sometimes brownish, and transparent. If it is turbid, this is due to admixture of acid gastric juice, or to admixture of white corpuscles. In icterus no bile was found, but all three pancreatic ferments were present. Repeated absence of bile testifies to complete obstruction of the common bile duct. There is normally no mucus in the duodenal juice, which is alkaline, sometimes neutral in reaction, or even acid from admixture of gastric juice. Blood, when present, indicates ulcer. Microscopic examination shows the presence of pavement or cylindrical epithelium, neutrophiles, eosinophiles and some lymphocytes.

¹ Abstract Journal of American Medical Association, 1916, lxvi, 850.

² *Ibid.*, lxv, 1226.

MECHANISM OF REGURGITATION OF DUODENAL CONTENTS INTO STOMACH. Boldyreff, in 1904, published in Russian, and in a later article (1914) stated that when oil and acid are introduced into the stomach, duodenal regurgitation takes place by a mechanism of its own. This was the first instance in which antiperistalsis had been reported as a normal motor activity of any part of the gastro-intestinal tract, according to Hicks and Visser.¹ These authors have not been able to confirm Boldyreff's statement, and they agree with Starling and with Cannon that "an antiperistalsis is never observed in the small intestine.

Duodenal Feeding. In Jones² article he states that in some of his cases, from twelve hours to seven days is required before the tube enters the duodenum, but, surprising as this statement is, it is recalled that he is speaking of cases of extreme ptosis and hypomotility. If it takes longer than twelve hours for the tube to pass the pylorus, feeding is begun as though the tube had not been introduced. In one case the ptosis was so extreme that the tube failed to pass after more than two weeks. If the patient has an unusually sensitive throat, Jones dissolves a quarter grain cocaine hydrochloride in one dram of water, has the patient gargle with it and then swallow the solution.

The feeding is begun first with 2 ounces of milk every two hours, the rate of administration being from 60 to 120 drops per minute. On the second day the milk is increased to 4 ounces and so on, increasing 2 ounces each day up to 12 ounces every two hours, from 8 A.M. to 8 P.M. Then the white of an egg is put in every second feeding, next, the white of an egg to every other feeding, then a whole egg to every feeding. If there is no excessive putrefaction, evidenced by the feces or distention by gas, the food is increased, giving first a milk of 6 per cent. butter-fat, then increasing to 8 and 10 per cent., and finally increasing the eggs to twelve or fourteen a day, and the 10 per cent. milk to 120 to 128 ounces in twenty-four hours. In most instances the food in such quantities is well borne, even in cases which do not increase in weight under the treatment. The milk and eggs must be strained through three or four thicknesses of fine linen, so as to remove any clot of milk or eggs which might obstruct the tube. When there is any discomfort from the milk, it may be diluted with water and citrate of soda added, one grain to the ounce.

Gross and Held³ recommend the use of a larger tube than the Einhorn tube, and also give the feedings somewhat differently from the method advocated by Jones. The first three days, 250 c.c. of milk, to which 15 grams of glucose are added, are given every two hours. This yields 1528 calories. On the fourth day, yolk of egg is added to the milk three times a day, an additional 174 calories, bringing the total in twenty-four hours to 1702 calories. If this is well tolerated, one can, on the fifth or sixth

¹ American Journal of Physiology, 1915, xxxix, 1.

² Surgery, Gynecology and Obstetrics, 1916, p. 236.

³ Journal of American Medical Association, 1915, lxx, 520.

day, add a yolk of an egg to each feeding, supplying 232 additional calories, or a total of 1934 calories. On the seventh day the entire egg is added to three feedings, the other feedings remaining the same, total calories being 1955. If this is well borne, an egg to each feeding is given on the eighth day—a total of 2053 calories. On the ninth day one tablespoonful of cream is added to each feeding, 2350 calories in twenty-four hours, and this is continued until the duodenal alimentation is completed or until the end of the fourteenth day.

The authors maintain that duodenal feeding has by no means replaced the well-established methods of treatment of gastric and duodenal ulcer. If, however, an ulcer treatment conscientiously carried out for one week does not relieve the symptoms at all, duodenal feeding is instituted. After the tube is removed the patient must not be allowed immediately a liberal diet, even though he has no symptoms. The first two days after the tube is removed the patient receives milk with sweet cream and six eggs daily. On the third day toast and butter and fine cereals are added. On the sixth day the diet corresponding to the third week of the von Leube treatment is begun, and continued with the von Leube treatment until the end of the sixth week. Five days after removal of the tube, the patient is allowed to resume business. Should it happen that the symptoms recur when the patient takes a more liberal diet, the fluid diet is resumed for a few days, and if this is ineffective, another course of duodenal feeding may be tried for a week.

Primary Carcinoma of the Duodenum. Forgue and Chavin¹ claim that cancer of the duodenum may be divided clinically, symptomatologically, and pathologically into three types, periampullary, supra-ampullary and infra-ampullary, depending on whether the tumor is situated at the ampulla of Vater, or above or below the same. A complete historical review is given of duodenal cancer, which was first described, in 1746, by Hamberger. This part of the article under discussion, is of importance, of course, but, for divers reasons, I shall leave it undiscussed.

I. ETIOLOGY. (a) *Frequency.* It is an undeniable fact that cancer of the duodenum is rare, and just what proportion of intestinal cancers occurs in the duodenum it is difficult to state, possibly due to the fact that the diagnosis is not easily made. Earlier writers have asserted that carcinoma in this locality is more frequent than in any portion of the intestinal tract, notably Neumann and Birsch-Hirschfeld, the last named, however, in later years, revised this opinion. A summary of all the statistics quoted by Forgue and Chavin shows the following incidence; in 83,031 autopsies, cancer was found 6817 times, and, of these, 642 were of the intestines, the large intestine being affected 603 times (94 per cent.) and the small intestine 39 times (6 per cent.). Or, in other words, cancer of the intestine was found in 0.7 per cent. of all cancers.

¹ Revue de Chir., 1915, xliv, 470.

Other statistics have been collected from Labbert, Fleur, Hausmann, Kohler, Ruep, Nothnagel, Müller, Geiser and Ménétrier, which give 888 cancers of the intestine, divided as follows:

Large intestine	798	90.1 per cent.
Small intestine	91	9.9 "
Duodenum	42	4.5 "

or about 0.34 per cent. of cancers in general occur in the duodenum.

Sarcoma seems to have a preference for the small intestine, while carcinoma is more frequent in the large intestine.

(b) *Predisposing Causes.* The relation of sex to duodenal neoplasm is a cause for some debate, but Forgue and Chavin from their own small number of cases and from the writings of previous observers, merely state that cancer of the duodenum is more frequent in men than in woman.

As far as age is concerned, all writers are united in saying that the affliction is one of adult life, even of old age, the mean age being fifty years (Pick). Forgue and Chavin discriminate between sarcoma and carcinoma, and although sarcoma is seen generally in early life, it would be a mistake to conclude that it is a disease of the young. The following table is of interest:

Below 10 years	1	} sarcoma
From 11 to 20	2	
From 21 to 30	4	
From 31 to 40	5	} 5 sarcomas
From 41 to 50	5	
From 51 to 60	7	
From 61 to 65	6	} 12 carcinomas
From 66 to 70	6	
From 70 to 80	2	
Above 80	2	

Heredity plays no appreciable role, and Forgue and Chavin, in 45 observations, have found no cancerous history in antecedents of the patients.

(c) *Local Predisposing Causes* are of two classes, the one anatomical, and the other pathological. Among the first are placed the flexures, constrictions and dilatations normally seen in the duodenum, and among the second are put mechanical, chemical or infectious lesions of the intestines. We know that the localization of choice for intestinal neoplasms is at the place where there is constriction or normal angulation, at which place there is certain to be more strain or wear and tear exerted. Forgue and Chavin draw analogies between the structure of the duodenum and other portions of the intestine, and furthermore emphasize the fact that the duodenum is the most firmly fixed part of the gut. The first portion of the duodenum being endowed with greater mobility than

the other part, it is here that most strain occurs. Apart from these structural moments or mechanical causes there are certain pathological conditions which no doubt play a prominent role.

Biliary calculus must be incriminated in the production of cancer of the ampulla of Vater. At this place calculi are shoved along through the narrowest portion of the biliary passages, and a further obstruction is afforded by the sphincter of Oddi which closes down on any obstacle. These two factors tend to produce diverse epithelial lesions, and these repeated irritations are no doubt concerned in the production of malignant neoplasms. It would seem that once entering the relatively vast canal of the intestine, further irritation would cease, but the authors contend this is not entirely true, as there is bound to be more or less irritation wherever the normal angulations are found, particularly at the duodenojejunal angle.

Ulcer of the duodenum is concerned particularly in the production of supra-ampullary cancers. Henlin says: "No one has yet reported an instance of duodenal cancer arising on the site of ulcer, but it is most probable that it will be met with one day, analogous to the production of gastric cancer on the basis of an ulcer." Since then Ewald described such a case, and followed it, in 1896, with another. Schröter, in 1887, Mackensie, in 1892, and Lebulle, in 1897, have all reported cases. The best and the most complete anatomical description is that of Letulle; although but few cases of cancer from such a cause have been published, the possibility of this etiological factor can be denied, but Forgue and Chavin warn against mistaking an accessory pancreas for duodenal cancer. Indeed, in Schüler's case it is by no means proven that the duodenal cancer did not arise from an accessory pancreas which was coexistent with the cancer.

II. PATHOLOGICAL ANATOMY. Under this heading the authors describe in great detail tumors found in this region, cancerous tumors, their study embracing their own observations and those of previous writers. Forgue and Chavin draw nice distinctions as to what should be regarded as the limits of the ampulla of Vater, limits not possible to recognize anatomically. Since macroscopic and microscopic examination leave one in the lurch, they make a distinction which they call "*définition anatomo-clinique*." Cancer of the ampulla has a precocious symptomatology, and is accompanied by serious disturbances incompatible with long life. Thus, anatomically, it is a cancer of small volume, because at operation or at autopsy it is seen in an early stage of development. It rapidly causes obstruction of the biliary and pancreatic passages, expressed clinically by icterus and pancreatic insufficiency. Intestinal symptoms are seen later. Forgue and Chavin, therefore, recognize as purely ampullary those cancers whose symptomatology is entirely hepatic or pancreatic. It is of slight importance if their point of origin was periampullary. On the other hand, they regard as cancers of the

duodenum all those extensive cancers even if they have invaded the ampulla of Vater. In order not to bandy words, the authors suggest that cancers of the ampulla be called periampullary cancers.

Carcinoma of the duodenum may be classed in two groups, the first comprising cases originating above the papilla, and giving rise to symptoms resembling pyloric stenosis. The stenosis is generally above the bile passages, so for this reason absence of bile in the vomitus is an important sign. In the second group are placed cancers below the ampulla, giving rise to symptoms of pyloric stenosis associated with bilious vomitus. These two groups of cases are designated as supra- and infra-ampullary cancer.

The microscopic appearance of duodenal cancer varies under different conditions, and the structural peculiarities are thoroughly described. When progression of the growth occurs, the pancreas is the first structure to be invaded, and, after this, the bile passages, particularly the common duct and cystic duct. Metastases occur more frequently in cancer of the duodenum than in cancer of the ampulla of Vater, and apparently even the smallest cancers are accompanied by widely distributed metastatic growths. Invasion of the glands in the pancreaticoduodenal angle is common, also the retroperitoneal glands, those along the aorta, the mesenteric glands, the peritoneum itself.

III. SYMPTOMS. The diversity of symptoms may be understood when one recalls that in its development duodenal cancer may attack the digestive tract, the biliary tract, or the pancreatic duct. According to the case, there may be ulceration, more or less hemorrhage, or a stenosis more or less complete and progressive. According to its anatomy, the tumor may be readily palpable or may escape the most rigid examination. According to its more or less serious metastatic activities, it may exhibit a symptomatology defying all classification.

The onset is generally hailed by the exhibition of icterus, that is, when the cancer is of the ampulla; in such cases the symptomatology is essentially hepatic. In true duodenal cancers, symptoms are rather gastro-intestinal in nature. Vague dyspeptic symptoms are described, loss of appetite, or anorexia, indigestion, weight in the epigastric region and malaise after eating. Vomiting may be early or may be delayed. Diarrhea, or exquisite abdominal pain, resembling tabetic crises, are commonly associated with the vomiting. In some instances, pain is the primary and cardinal symptom. Intestinal obstruction may be wrongly diagnosed in the presence of vomiting, pain and obstinate constipation. The beginning of the trouble is thus seen to be variable, at times it is slow and insidious, at other times it is brusque and acute; at times it manifests itself by functional disturbances, or by physical signs, or by general signs of ill health. The functional troubles most commonly seen are those of the digestive tract, anorexia, nausea, vomiting, constipation, diarrhea, and pain.

Anorexia is seen early, and with this is seen gastritis hypochlorhydria. Vomiting occurs frequently, and the amount vomited is generally large. At first, vomiting takes place two or three hours after eating, and the vomitus consists of the food which has been eaten, diluted with serous liquid. There is generally no hydrochloric acid present. Later, gastric dilatation appears, enormous amounts of material are vomited and the picture becomes now that of pyloric stenosis. Rarely, blood is observed, but when bile is present it is almost certainly a sure indication of infra-ampullary cancer.

The pain, which occurs later, is variable in its manifestations. It is variously described ranging from a sensation of mere oppression to pain which is not unlike that encountered in tabes. Pain is a characteristic symptom but is by no means constantly seen, as cases have been described where there has been comparatively little discomfort. The explanations for the pain are as varied as the pain itself. (1) due to compression of the celiac plexus by the tumor itself; (2) due to distention of capsule of the liver by the biliary stasis; (3) due to adhesions; (4) due to efforts of intestine to overcome the obstruction.

Intestinal troubles form an important part in the symptomatology, although they occupy by no means as prominent a place as do the digestive symptoms. Diarrhea is infrequent; normal stools have been observed, but, as a rule, constipation is a feature. Sometimes the stools are light in color, and sometimes they are richly stained with bile; when there has been hemorrhage, the feces assume a color resembling coffee. Owing to the repeated vomiting, thirst is a troublesome feature. The urine soon becomes scanty, albuminous, and contains bile when icterus is present. Attention has been drawn to the presence of indican, but conclusions deduced from this wily chemical body should be arrived at very cautiously. Hiccoughs are met with very frequently.

PHYSICAL SIGNS. The physical signs alone permit of the true diagnosis, and the most important are: (1) tumor; (2) gastric dilatation; (3) condition of the abdomen; (4) condition of the gall-bladder, and the presence of icterus; (5) adenopathy; (6) gastric chemistry; (7) x-ray.

1. Generally, the tumor consists of merely a constriction about the duodenum, and rarely gives rise to an appreciable tumor. However, the secondary glandular enlargement may be so great that a mass may be detected. The tumor mass is generally irregular in shape, it may be nodulated, and hard in consistency. The location of the tumor varies, although usually it is about the umbilicus in the epigastric region. It may present itself below the umbilicus and invade the hypochondrium, and it may occupy the entire epigastrium, the right hypochondrium, the right flank and even the lumbar region. It is rare to see a tumor of small size situated at the right of the umbilicus. Few authors mention the degree of movability, but those who do, describe it as possessing respiratory movability and palpatomy movability as well. It is probably

true that at the onset the tumor is freely movable, but that later it becomes fixed to the adjacent organs.

2. The *gastric dilatation* is an important sign; it may be recognized merely by inspection, percussion appreciates it, and upon shaking the patient, a succussion splash is clearly heard. Even the duodenum may suffer dilatation, and if the pylorus is relatively patulous, all the signs will be found in the duodenal region. After careful lavage of the stomach, one may find in a short time that organ filled with intestinal contents and serous liquid, clinically expressed in profuse vomiting.

3. *Abdominal Examination.* This is important, as it reveals the presence of nodules in the omentum, peritoneum or in the liver. Ascites is frequently found and is detected by the usual physical signs. Usually the abdomen is flattened and flaccid, serving to distinguish duodenal cancer from low intestinal obstruction which usually gives rise to abdominal distention.

4. *Signs of biliary stenosis* are rarer in cancer of the duodenum than in ampullary carcinoma. Icterus is a frequent finding. Courvoisier's law holds here, in a way, namely, when the gall-bladder is small it speaks for gall-stones, when distended, for tumor.

5. *Adenopathy* is frequent, but since the retroperitoneal glands are generally the ones to be involved, glandular enlargement may escape detection.

6. *Gastric Chemistry.* Examination of the gastric contents reveals the presence of bile and pancreatic juice. The gastric acidity is very variable, but has a tendency to be low.

7. The *x-ray* is of vital importance, but Fergue and Chauvin find no mention of it by other writers.

IV. EVOLUTION. *Complications. Prognosis.* Duodenal cancer is progressively fatal, but just how long the clinical course is, is difficult to say, as in many instances the onset is insidious. The tumor may be latent, until suddenly it erupts into activity, and the patient succumbs in a short time. As a rule, the clinical course may be divided into two periods: In the first, of relative latency, vague dyspeptic symptoms are seen, such as have been described above. In the second period, vomiting appears, the stomach is dilated, and one sees the picture of pyloric or of intestinal stenosis. Bloody vomit or melena may appear, the tumor becomes palpable, and the cachectic state becomes pronounced. It is generally in the second period that the patient comes under observation, and, later, edema appears, ascites and phlegmasiae alba dolens. The duration of the trouble from the time of onset is, on the average, from six to eight months (Pick), but our authors state, from their personal observation, that there is no mean, but that the disease may be from a few days to two years' duration.

Complications are rare, excluding metastases. Peri-intestinal abscess has been reported, adhesions and later fistulae are seen, hydronephrosis

from compression of a ureter; phlebitis has been observed in the femoral, hypogastric, iliac, and inferior vena cava. The tumor may invade an artery and give rise to fatal hemorrhages. Necrosis of neighboring organs has been described.

V. CLINICAL FORMS. (a) *Supra-ampullary Cancer*. In this the onset is insidious, as is often the case with gastric cancer. Other signs may be seen of pyloric obstruction from whatever cause, but an important feature of the vomiting is the absence of bile, of pancreatic juice and of blood. Theoretically, the tumor should be palpable, but practically this is not the case. In short, the symptoms of duodenal cancer resemble very closely those of pyloric tumor.

(b) *Infra-ampullary Cancer*. Here the symptomatology is more distinctive. The disease has a longer latent period, and reacts more slowly on the digestive tract. When stenosis finally appears, symptoms are more mild and the course is more slow. The most characteristic symptom is vomiting, which is rarely so violent and is infrequently so profuse as in the supra-ampullary cancer. Bile is present, and also pancreatic secretion.

(c) *Sarcoma of the Duodenum*. Sarcoma is seen generally in young individuals. The tumor grows to an enormous size, occupying the whole abdominal cavity, and may be mistaken for an ovarian cyst.

I have found this article of Fargue and Chauvin most instructive, and well worth the number of pages this abstract has occupied. It has always been of much interest to know why cancer of the duodenum, on the basis of ulcer, is so rare, while cancer on the basis of gastric ulcer is so frequent. The authors have stated that it does occur, but out of all proportion to the number of cases of duodenal ulcer which have been observed. Discussion of this point is not made by the authors, and one would have wished for more enlightenment. Nevertheless, this article is extremely important, and leaves but little to be desired on the subject of duodenal cancer.

Movements of the Colon. Walsham and Overend¹ state: "In the normal individual a shadow appears in the ileocolic region within four hours after the administration of an opaque meal, and when an interval of eight hours has elapsed, this opacity has left the ileum and is contained altogether in the colon. Entering the latter intermittently, it drops into the cecum, gradually filling it and the appendix. The ascending colon becomes progressively distended and eventually a wave of peristalsis arises which drives some of the chyme into the transverse colon. This initiates waves of antiperistalsis which, starting in the proximal part of the transversum, pass down the ascending colon, distending the cecum and appendix, and inaugurating new waves of peristalsis. These finally succeed in carrying the food into the distal transversum. The

¹ Archives of Radiology and Electrotherapy, 1916, clxxxvi, 260.

advancing wave reaches the latter in six hours, the splenic flexure in nine, and the brim of the pelvis or ileopelvic junction in eleven hours. Practically, the whole of the bismuth may be collected within the distal part of the pelvic colon and the superior or pelvic chamber of the rectum after eighteen hours. In this situation it forms a large ovoid mass, the pelvic residuum. The greatest length of the opacity is reached about the twelfth hour. It then appears continuous nearly as far as the umbilicus; beyond this point it is discontinuous and forms short, separate fragments. Retrograde movements are most common in the ascendens but they have been observed near the termination of the distal transversum, and at the commencement of the pelvic colon. Although the major part of the bismuth after twenty-four hours has accumulated within the rectopelvic junction, we may still find traces within the cal-ascendens, the transversum and the descendens.

"On the screen, to the naked eye, apart from the passive movements due to respiration, the opaque colon is perfectly motionless. But, if radiograms are taken at intervals of ten minutes, an incessant change in the outline of the shadow may be perceived. This accounts for the blurring of the shadow often seen with exposure lasting more than a few seconds. The excursions are minimal, are due to contractions of the circular muscle, and serve for the kneading, mixing and churning of the contents. In the lower mammals, these rhythmic contractions occur at the rate of about twelve times per minute. They possess no directive power, although they may exhibit periodic augmentation. Whether they are purely myogenic, or myoneurogenic in origin, in the latter case dependent on the activity of the myenteric plexus, is still *sub judice*. If they are to be ascribed to the latter, this plexus, as we shall presently see, must be endowed with a double rhythm. They have been named small, continuous, segmental movements.

"The anterograde movement of the chyme is due to a true peristalsis, that is, to a wave of contraction preceded in part by a wave of dilatation. This has been termed diastalsis. The contractions occur at the rate of one or two per minute, and are attributed to the nodal tissues, since in the lower animals they are abolished by nicotine and curare. They correspond, apparently, to what has been recently termed isomorphous haustration. Although invisible to the naked eye, if the patient be examined again at the interval of an hour, an advance of the shadow may be detected, even if neither food nor drink has been taken in the meantime. Seeing that they must be accompanied by a dilatation in front, they may be termed microdiastaltic movements.

"In addition to the above, there is a third which is associated with the transport of chyme over a considerable distance of the colon. These have been designated movements *en masse*, or sporadic large movements. They generally occur after the larger meals, and are obviously closely connected with the inception of food and the evacuation of the

bowel. As such they will take place at least three times a day, and they appear to last only a few seconds on each occasion. On this account they are rarely seen. Now the vagus, possibly the pelvic nerve also, contain two sets of fibers, one inhibitory with a short latency of one second, and a second, augmentory with a latent period above ten seconds. The initial inhibiting effect is produced equally on both longitudinal and circular muscular coats. The subsequent augmentation is confined to the circular muscle alone. We can therefore understand the phenomena presented by the movement *en masse*. First, one ovoid or sausage-shaped figure appears, in which haustral segmentation vanishes, this is obviously the result of the relaxation of longitudinal fibers. The advancing margin is broad and tapers off gradually. Within it a ring or annular constriction becomes visible, which pursues the dilatation and drives the contents forward. Behind it a very thin line of bismuth may be left, the expression of a small constricted lumen. This is obviously produced by the contraction of the circular fibers. As the wave ceases, the longitudinal fibers pass again into the usual tonic condition and the haustra reappears. They may be termed megadiastaltic movements. We may assume that the movement for the ascending colon and proximal transversum will start at the ileocolic node, as the result of a gastrocolic or rectocolic from the sympathetic in the vagopelvic nerve. With its retinacula or some residue of the sphincteric tract of the lower mammalia, the valve will provide a *point d'appui*. If it is essential that the cecum should never be completely evacuated, the megadiastaltic activity should commence at the level of the valve and leave the body and tip of the cecum free. The wave would increase in amplitude and intensity as it approaches the hepatic flexure just as gastric movements commencing beneath the fornix or air reservoir become more obvious as they reach the pyloric half of the stomach. Also, the megadiastaltic movement has been seen to start near the end of the transverse colon and sweep the contents round the splenic flexure, down to the descendo-iliac into the pelvic colon. Possibly this is due to the reflex activity of the pelvic nerve. For rapid transit there must be coördination between the vagus and pelvic nerves. These nerves are connected with the proximal and distal rhythmical zones of the colon respectively. Movements of a similar nature may be readily observed by the injection of salt or soap enemata containing barium.

"The occurrence of antiperistaltic movements in man as a physiological actuality is still a matter of doubt. According to Case, whose opportunities of observation have been unique, they appear to start at the sphincter in the transversum already mentioned, and to pass down the ascendens toward the cecum. Indirect evidence has been adduced as to their existence in the distal colon. If the statement of Case be verified, that they correspond in all directions to the

movements *en masse*, anastalsis in man must be a true reverse peristalsis, and must differ from the movement in the lower mammalia. The frequency of anastalsis in the proximal colon must promote the function of the latter as an organ of digestion and absorption. Moreover, just as there are meganastaltic movements, there may be micro-anastaltic also. The formation of the movements will depend on the presence of a higher potential within a distal nodal area. Anastalsis, when exaggerated, is a sign of obstruction lower down, accompanied by an increased excitability of myenteric tissue in the same locality, and must therefore be expected to occur frequently in spastic constipation as in stenosis due to innocent or malignant growths.

"A fifth variety of movements of the colon is seen in the large pendular or swinging movement. Occasionally radiograms are obtained, in which, although the patient has been photographed under exactly the same conditions as before, the situation of the transverse colon differs considerably in the two.

"There may be a possible mechanical explanation of this alteration of site; on the other hand, the deviation may be produced by spasm, or relaxation of the band of unstriped muscle which run in the folds of the mesocolon."

Motor Functions of the Intestines. Alvarez¹ conceives the intestinal tract as a tube with greater tone and rhythmicity at the oral end. It is apparent that a rise of tone at the upper end would hurry the aboral progress of food; while a similar rise at the lower end should slow the current and even reverse it. A rise anywhere in the middle of the tube should cause material to flow both ways from that point. Hence it is that food goes down the tract more easily because it is put in at the upper end (Alvarez is well aware of the Hibernian nature of this remark) because the rise of tone then probably makes the gradient of forces steeper down the intestine. Furthermore, the passage of food will be accelerated through the bowel if followed by more food a few hours later, probably because this second meal keeps the gradient steeper than usual by maintaining the high level of the gastric tone.

Pleasurable psychic stimuli raise the tone, and meals leave the stomach more quickly if more palatable. He calls attention to the clinical observation that patients who have vomited while on a liquid diet, may cease this when solid food is administered. (Alvarez suggests that vomiting is often a manifestation of reversed currents, due to an abnormally high tone in the jejunum.) Liquids (water) would not have much effect on gastric tone as they pass rapidly into the intestine, but solid food can restore the normal gradient and currents are sent downward once more.

It would seem impossible to explain the peculiarities of gastric

¹ Journal of American Medical Association, 1915, lxy, 388.

emptying with gastric or duodenal ulcer, on the basis of chemical reflex alone, for it has been demonstrated how little connection there is between the degrees of acidity and the rates of emptying in individual cases. Gastric emptying may be delayed by means other than food, for the emptying time of the stomach may be retarded for hours by mechanical distention of the duodenum, by irritation of the bowel by strong saline solutions. We can comprehend this phenomena if we think of the intestinal tone as having been raised above that of the stomach. When the tone falls as a result of bowel emptying, the stomach can again empty itself.

The ill-effects, in some individuals, of eating between meals is due to the slowing of gastric evacuation by the presence of the previous meal in the small bowel, and it has been observed frequently that when the tone of the intestine is high and that of the stomach is low, there is a regurgitation of duodenal contents into the stomach. Fat causes this regurgitation and has been utilized as a means of recovering intestinal ferments. The explanation of this lies in the fact that, while the tone and motility of the stomach are lowered, the intestine may be stimulated by the presence of fatty acids. In duodenal ulcer, late emptying of the stomach is characteristic, and Alvarez believes in these cases the increased tone of the stomach overcomes the hypertonic duodenum and brings about rapid emptying at the beginning, but after this a small residue remains in the stomach for hours because the ulcer keeps the duodenum from relaxing to its tone level, which is below that of the stomach.

If this theory be correct, food introduced at the lower end of the tract should delay or even reverse food coming from above. Clinicians recognize this, for colic, nausea, and even vomiting frequently result if an enema is given shortly after a meal. Alvarez quotes from his own experience, and from that of others, to prove how frequently this may result.

When food is put into the middle of the bowel it tends to move both ways, although experience with jejunal feeding have not been entirely satisfactory on account of the nausea and vomiting. Food introduced through a jejunal fistula may be returned by mouth, but this may be prevented by simultaneous mouth feedings, which presumably raised the tone of the stomach above that of the jejunum. Attention is called to the cessation of nausea, vomiting and pain incident to jejunal feeding, following Murphy drip of glucose and salt solution. Vomiting is often associated with diarrhea, food passing both ways. Probably the tone of the jejunum is raised above that of the stomach to prevent it from emptying; finally, the tone becomes high enough in the upper bowel so that it can clear itself both ways.

Irritant lesions of the tract affect its motility. In gastric ulcer, the stomach is often quiet and atonic because the waves are blocked

by the tonus ring caused by the lesion. Even actual reverse waves are seen, particularly when the bismuth is taken when there are remains of the previous meal in the intestine. Lesions in the bowel itself irritate the affected area to such an extent that the meal goes through very quickly, and the region appears empty. Appendicitis disturbs digestion by raising the tone of the terminal ileum, and its effects are removed when the source of irritation is withdrawn. Gastric dilatation is an early sign of intestinal obstruction and is a case in point.

Constipation may cause vomiting, and these patients feel stuffed even after a few mouthfuls. Alvarez likens the condition to baseball, when the bases are full and the batter has made a hit, there is no use of his running if the runner on third refuses to come "home." He believes a large part of what is termed "biliousness" and "auto-intoxication" may be due to reverse peristalsis when the colon remains filled and active, and much of the satisfaction derived from calomel in the bilious may be due to the setting of a strong current down the tract again. The auto-intoxicated individual feels relieved within a few minutes after emptying the rectum—no toxin could be so rapidly eliminated. Normally, the tone of the rectum and sigmoid is higher than that of the cecum and ascending colon, which operates to keep feces out of the ampulla except when the pressure in the upper part of the tract is very great. Constipation is probably an expression of increase of this tone, making the gradient steeper up to the rectum. Hemorrhoids and painful fissures may act in this way.

The reader is referred to the article by Keith on Intestinal Stasis, where the theory of nodes is given exposition.

Intestinal Stasis. The article by Keith,¹ in which a new theory of the causation of enterostasis is detailed, is attracting a great deal of attention and provoking much discussion. In previous numbers of *PROGRESSIVE MEDICINE* we have given full consideration to enterostasis, for we agree with Keith, who says, that it is a condition which causes nearly as much suffering as a great war, and each year the subject has been followed step by step. This year the article of Keith illuminates the field, and since it is the most brilliant effort in this direction, we propose to devote much space to its consideration.

There are certain points of the alimentary canal where food is normally delayed, at the junction of the esophagus with the stomach; at the junction of stomach and duodenum, there is one which affects a prolonged delay of the gastric contents; there is a regulating mechanism near the duodenojejunal junction; there is one at the lower end of the ileum. In the large intestine there are three points at which delay is normal: (1) near the commencement of the transverse colon, leading to the filling of the cecum and ascending colon; (2) at the rectocolic

¹ *Lancet*, 1915, ii, 371.

junction, leading to accumulation in the pelvic colon; (3) above the anal canal, leading to accumulation in the rectum. In different individuals the time of delay at these different points varies, but, apart from these individual peculiarities, there are certain persons in whom the delay must be regarded as pathological. If "ileal stasis," "duodenal stasis," "gastric stasis," "proximal colonic stasis," "distal colonic stasis" are terms, why not "esophageal stasis" and "rectal stasis?"

Keith's work on enterostasis had its commencement in a study of the ileocecal region with the object of throwing more light on that system of tissues in which the heart beat arises, but with no thought of enterostasis in mind. The ileocecal region was selected because lively and complex movements had their origin there, and Keith inferred that if a special tissue, representing the nodal tissue of the heart, were present in the bowel, it should be found in the ileocecal region. In the rat there was found a collar of peculiar tissue, having two extensions passing into the anterior and posterior walls of the cecum. In the collar were nerve cells and nerve fibers, but there were, in addition, numerous branching cells uniting with muscle cells and with ganglionic cells. This arrangement represented then the nodal heart tissue, and the ileocolic band, or collar, was but a local specialization of the myenteric or Auerbach's plexus.

A study of the myenteric plexus in man and in the lower animals convinced Keith that this plexus was not a simple collection of nerve cells and nerve fibers, but was of a complex structure. There are ganglion cells in the plexus, and there is a network of very fine fibers, also a third element, branching intermediate cells, mentioned above. In the plexus the muscle cell and the intermediate branched cell resemble each other so closely that it is sometimes difficult to differentiate them. This plexus represents a nodal as well as a conducting system, and Keith believes the intermediate branched cell, which has such a close resemblance to nerve and muscle elements, can assume the function of either. If the hypothesis that the myenteric plexus represents in the intestine a system corresponding to the nodal and conducting system of the heart, then a similar manner of development should be presupposed. It has been found that the myenteric plexus arises in a manner corresponding to the bundle system of the heart, which arises from the muscle-forming stratum beneath the endocardium. Section of the fetal intestine clearly shows the longitudinal and circular muscular coats separated by an intermediate cell layer, which is definitely myogenic in nature, and it is from this that the myenteric plexus is developed. Hence another link is welded in the chain of evidence that the heart and intestines have corresponding functional structures, this link being the proof that the manner of development of the nodal systems in both structures is the same.

Other parts of the alimentary tract were examined. In the stomach

it is held almost unanimously that the peristaltic waves which sweep along the pyloric part of the stomach arise in the distal or lower part of the stomach. The myenteric plexus was found to be well developed in the pyloric division of the stomach and along the lesser curvature, but along the greater part of the stomach and in the fundus the plexus was less abundant. Examination failed to reveal any nodal system at the point where gastric movements appear to take their origin. Since the search in the stomach led to negative results, and since the ileocolic collar mentioned above seems to be part of a sphincteric mechanism, the various sphincteric regions of the alimentary tract were next studied.

The cardia of the stomach showed a distinct modification of the musculature and myenteric plexus just distal to the ring which marks the cessation of the esophageal epithelium and the commencement of the gastric lining. At this point there was a tissue which might well serve as a nodal center for the stomach. Comparative anatomy confirmed this view. Stimulation of this nodal center provoked a definite form of gastric movement. The movement commenced with a contraction of the musculature of the stomach adjacent to the cardia, and spread along the lesser curvature to the hiatus angularis, where it ceased. The fundus and the greater curvature were not involved. Each cardiac movement was followed by a peristaltic movement along the pyloric portion of the stomach, corresponding to the waves described by röntgenologists. This seems proof incontrovertible that there is a main nodal center at the gastro-esophageal junction, at which contractions of the stomach are normally initiated.

In the duodenum there is a rich development of the myenteric plexus in the neighborhood of the ampulla of Vater. The nerve tissue from the solar plexus formed union with it, and the ampullary sphincter was supplied from this myenteric tissue. In the first or horizontal portion of the duodenum the myenteric plexus is poorly developed, the strands apparently being direct extensions from the sphincter region in the stomach. In the second part of the duodenum, however, the plexus is richly developed, especially in that region against which the head of the pancreas lies. Keith refrains from asserting that a duodenal center has been found, but suggests that if one be located it will be discovered in the second portion of the duodenum proximal to the entrance of the common bile duct.

In the colon the plexus was plentiful in the distal part of the transverse colon and in the descending and ascending colons. It is well developed in the rectum. Nowhere was there any special area for nodal tissue, but everywhere there was an abundance of intermediary cells.

Keith offers argument against the mechanical conception of enterostasis, calling to his aid the Röntgen rays, which fail to substantiate the claims of the mechanists. Transferring from the heart to the

alimentary tract the anatomical and physiological data relating to the nodal and conducting system, as well as the knowledge of cardiac pathology (heart-block, fibrillation, extrasystole, delayed conductivity), he believes a rational explanation of the motor derangement of the alimentary tract may be had. The intrinsic beat of bowel muscle has been demonstrated, a double beat or rhythm has been shown, the rapid beat producing ten to twenty contraction waves a minute, and a slow one with waves occurring one or two a minute. The slow beats gave rise to true peristaltic waves, the faster beats had to do with the mixing of the intestinal contents.

The inherent power of rhythmical contraction decreases as we pass along the duodenal loop; at the commencement of the jejunum there is an enhanced power which decreases as one descends to the terminal part of the ileum. There is a new zone at the ileocolic junction, and the ileocolic collar probably represents the pace-maker of the proximal colon. This zone extends, presumably, beyond the hepatic flexure into the transverse colon. Concerning antiperistaltic waves, Keith remarks that these are possible only when a distal center has gained an ascendancy in excitability over the proximal center. He believes there are four rhythmical zones in the intestine—duodenal, jejuno-ileac, proximal colic, and a distal colic—and probably two more, a gastric and esophageal. He suggests that the cardiac nodal tissue is the pace-maker of the stomach.

Why is it that gastric waves do not encroach upon the duodenum, and dominate the duodenal rhythm? There is a direct bridge of musculature and of myenteric plexus, yet gastric waves do not pass beyond the pylorus, probably on account of the peculiar nature of sphincteric muscle. Sphincters normally are in a state of contraction, and hence must have an almost continuous refractory period, and hence sphincters serve as a natural block for contraction waves. The Bayliss Starling law is quoted to the effect that contraction of one segment of the bowel causes inhibition of contraction in the segment just distal to it.

KEITH'S THEORY OF INTESTINAL STASIS. I have attempted to review in a few pages this most admirable paper of Keith's, and hope that Keith's fundamental work has been clearly enough detailed to enable the reader to understand the author's conception of enterostasis. Certainly Keith's original article is clear enough, and should this review fail to satisfy the reader, he should go to the source for fuller information.

Each zone of the intestinal tract has its own pace-maker and its own rhythmicity. Such are found in the heart—an auricular and ventricular with the sino-auricular node, the master pace-maker. Since there is such a similarity between the nodal and conducting systems of the heart and alimentary canal, certain irregularities may be expected in the latter as well as in the former. Such irregularities or blocks should be found

at the points where one rhythmical zone passes into the succeeding zone, and indeed, it is just at these places that "blocks" are found, namely, at the gastro-esophageal junction; at the gastroduodenal junction; at the duodenojejunal and at the ileocolic junction.

To obtain an orderly propulsion of food, these various rhythmical zones must be closely coördinated in their activities, for it has been shown that disturbance in one segment upsets the rhythm in all the segments. One can understand, based on Keith's hypothesis, how stasis in the large intestine may be followed by ileal stasis, duodenal or gastric stasis, or how a disturbance of conductivity or excitability of any of the rhythmical zones may give rise to stasis in all.

Keith, in conclusion, writes, "My hypothesis, you will find, has a certain advantage over his (Lane's). In the first place, I bring into the foreground the musculature of the alimentary tract, which is recognized by all as the sole propelling power in the intestinal wall. In his theory a defect in the musculature of the bowel takes a very minor part in the causation of stasis. Further, my theory is the more in harmony with the appearances observed by clinicians and pathologists, and because it rests on a better basis of anatomical and physiological fact, I believe it will ultimately win."

The nodal theory of enterostasis *versus* the mechanical theory in one which promises to be a subject of much debate. That nodes exist has been shown, that certain nodes have the function of pace-makers to certain parts of the intestinal tract has been demonstrated, that interference with the coördinate activities of these individual nodes affects the rhythmicity of the function of the entire alimentary tract is evident, but is it equally clear just what force, or forces are at work to bring about these blocks or imperfections in conduction, which Keith believes to be accountable for enterostasis. What are the pathological conditions which bring about block of the gastric intestinal tract? Are these functional or organic in nature, or both?

Keith has examined the lesions to which the myenteric plexus is subject in cases of colitis and intestinal stasis, and has noted fibrotic changes in the muscular coat, as one sees in the myocardium of diseased hearts a fibrosis in which meshes of the myenteric plexus are often involved. Structural changes in the cellular elements of the plexus were present also. This means but little in Keith's theory, unless it can be shown that disease of the myenteric plexus caused the stasis in colitis, or if the changes in the plexus were secondary to the colitis or stasis. Nevertheless, we have to do with a theory far more ingenious, and bewilderingly seductive in comparison, than the somewhat coarse mechanical view of Lane, but whether Keith's hypothesis "ultimately wins," as he believes it will, the future must decide.

Although a great deal is said about Lane's kinks, Jackson's membranes, the bands of Reid, and the necessity of surgical interference,

Eggleston¹ contends that in the beginning of these cases the trouble is purely functional, and as a result of this functional stasis, a mild inflammatory condition is set up, expressed pathologically in adhesions of greater or less severity. The condition then is not a congenital one, and does not arise in infancy, but results from the habits of this present generation. Lack of education in the selection of proper food, the high tension under which we live, heedlessness in observing the calls of nature, all these are contributing causes of intestinal stasis.

In the early history of these cases no marked discomfort is complained of, apart from constipation. Sooner or later there comes a time when the individual recognizes that he is not in good condition. He suffers from headaches, his tongue becomes coated, his breath is foul, he is depressed mentally, and he seeks relief from cathartics. Satterlee,² who writes on the same subject, quotes lines from Burton's *Anatomy of Melancholy*, illustrating the mental symptoms of those afflicted:

"All my joys to this are folly
None so divine as Melancholy.
I'll change my state with any wretch,
Thou canst from gaol or dunghill fetch;
My pain, past cure, another Hell,
I may not in this torment dwell,
How, desperate, I hate this life;
Lend me a halter or a knife.
All my griefs to this are folly,
Naught so damned as Melancholy."

Since drugs used as cathartics are injurious to the intestinal mucous membrane, there comes a time when these measures cease to be efficacious, and the individual lapses into a state of chronic invalidism. Normal function is now out of the question, for the colon has become bound down by adhesions.

Proof of the injuriousness of the absorption of toxins is offered by therapy. A thorough purge is followed by immediate relief. Nature's defense against these toxins are three, and it is because of the body's ability to protect itself against invasion that restraint of bacterial activity is effected. The first of this triple line of defense may be said to be the intestinal mucosa, which protects by virtue of its secretions. The second line of defense is the liver, which conjugates the indol, skatol, and phenol with the sulphuric and glycuronic acids to form much less toxic products. The third line of defense is the glands of internal secretion.

When these defenses are broken down, the symptoms are augmented, there is loss of weight, chronic headache, disturbed appetite, furred

¹ Medical Record, 1916, lxxxix, 399.

² New York Medical Journal, 1915, ci, 1204.

tongue, melancholia and various phobias. In many cases cutaneous bronzing is exhibited. In some instances, tachycardia is seen and other symptoms of hyperthyroidism.

In treating such a condition, the first indication seems to be a diet which will stimulate peristalsis, lessen putrefaction and afford sufficient nutrition. Bulk is essential, but not when it is provided at the expense of its nutritive value. In atonic conditions physical measures are advantageous, massage, manual and mechanical movements and exercise. The introduction into the intestinal canal of lactic-acid-forming bacteria is beneficial in many instances. When there is colitis, colonic irrigations of salt solution, alkaline solution and oil soothe the inflamed mucous membrane and provide lubrication.

Surgical interference is rarely required except when there is definite obstructive symptoms. Eggleston quotes Clark as sharing this view, and Bainbridge as saying that not more than one out of ten or twenty patients should be compelled to seek surgical relief.

Satterlee offers further suggestions as to therapy. He recommends thorough purging with castor oil, and, following this, irrigations of ox-gall, or hydrogen peroxide. Laxatives are forbidden, except dietetic laxatives. Since atony of the colon is assumed in many cases, massage (not the ordinary message) and vibration of the colon are useful. In the spastic type, manipulation of the colon may be harmful. In these cases belladonna and small doses of iodine may be given, together with rest, and heat locally. Satterlee likes electricity and agar-agar but is not particularly enthusiastic about liquid paraffin. He makes a distinction between the foregoing cases and those in which ptosis is coexistent, while Eggleston says it makes little practical difference whether the intestines are in their normal position or not. He differs with Eggleston, too, in the question of surgery, for he believes there is a number of cases that will not end well without surgical intervention. He seems to be a firm believer in colon vaccines.

Smithies,¹ in the discussion of Ochsner's paper (which, by the way, I have left to be abstracted elsewhere in *PROGRESSIVE MEDICINE*), believes that, as far as intestinal stasis provides a distinct type of individual is concerned, this is out of the question. Smithies assails the toxemia theory, stating that "although Laue and his co-workers have laid a strong emphasis upon the unusual biochemical and bacteriological findings in the gut of individuals coming to operation, these observers have never produced by the administration of these 'poisons' in experimental animals, or humans, the general or local anatomical defects, which, diagnostically, they claim result from fecal stagnation and retention." He calls attention to the protective mechanism of the gut, and finds no evidence that in stasis the normal functions of the intestinal

¹ Surgery, Gynecology and Obstetrics, 1916, xxii, 57.

wall are permanently altered, or that this alteration could be directly ascribed to stasis.

As far as treatment is concerned, he inclines to surgery, only when non-surgical care has been productive of no good results, after a reasonable length of time.

Idiopathic Megacecum. Bassler¹ has met with this anomaly only three times in 1742 x-ray examinations of the abdomen. It is impossible to say whether true, idiopathic megacecum is congenital or acquired, as his patients were all of middle age, but Bassler is inclined to believe that it is an acquired condition, on the basis of an intestinal toxemia from bacterial activities. The symptomatology may be obscure.

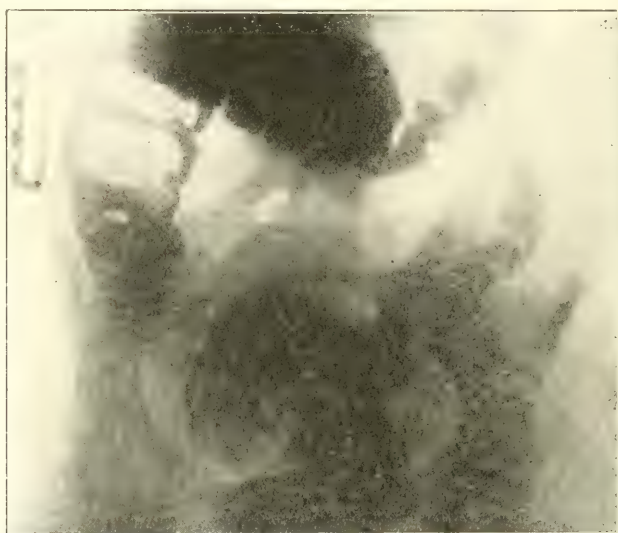


FIG. 25.—Mark on right side of patient. Note enlarged cecum involving about one-third of transverse colon, confirmed at operation. No obstruction at distal point of dilatation, but hypertrophied and thickened wall observed. (Bassler.)

Constipation is present, and there is a slight degree of fulness or distention of the right side of the abdomen, particularly noticeable when the abdominal walls are thin and relaxed. On percussion, pronounced tympany is encountered. Bassler claims that individuals with megacecum present the clinical picture of intestinal toxemia and that the laboratory examination of the stools and urine confirm this. I would direct the reader's attention to the original article of Smithies (see above), concerning the toxemia question. It is regrettable that Bassler has not stated what laboratory findings are confirmatory of toxemia, for I believe, personally, that the laboratory diagnosis of such a con-

¹ Journal of American Medical Association, 1915, lxiv, 1062.

dition is very difficult to make. Certainly indican, sulphates, urobilin, fatty acids and the phenol tests, as ordinarily applied, are of doubtful assistance. Perhaps the work of Folin on the quantitative estimation of phenol will prove to be of value.

Bassler gives cuts of the *x*-ray photographs which I reproduce here. Medical treatment was of great benefit, the patients becoming free of symptoms on medical measures alone. Massage was prescribed, sleeping with the foot of the bed elevated was ordered, a light fat and carbohydrate diet was ordained, and an evening dose of petrolatum, together with general nerve tonics, brought about improvement.

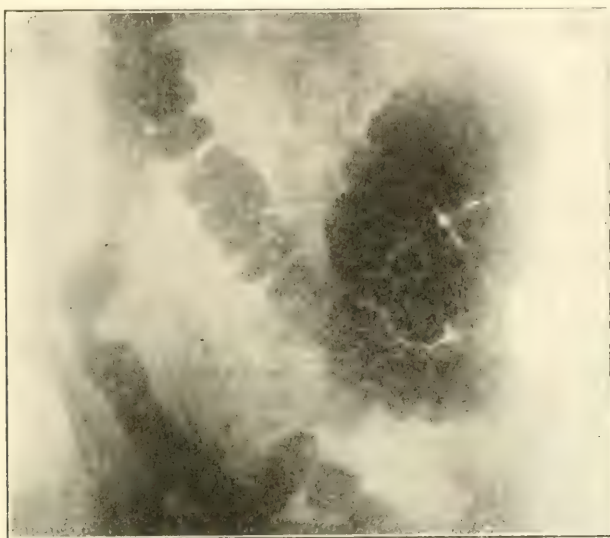


FIG. 26.—Mark on right side of patient. Note enlarged cecum involving about one-eighth of transverse colon. Confirmed at operation. No obstruction at distal point of dilatation, but hypertrophied and thickened wall observed. (Bassler.)

Intestinal Obstruction. NON-COAGULABLE BLOOD NITROGEN IN INTESTINAL OBSTRUCTION. The clinical observation of Tileston and Comfort (1914) that in man, intestinal obstruction is associated with very high non-coagulable nitrogen, has been confirmed by Cooke, Rodenbaugh and Whipple¹ in their experimental animals. With acute obstruction the rise in non-coagulable nitrogen may be rapid and reach as high as three, or even ten, times normal. With more chronic obstruction, there may be little or no rise. Clinically, this may have value, for a high reading means a grave intoxication, but a low reading may be observed in some fatal cases and gives no assurance that a fatal intoxication may not supervene.

¹ Journal Exper. Med., 1916, xxiii, 717.

Proteose Intoxication in Intestinal Obstruction. "A definite intoxication develops as a result of a closed intestinal loop and toxic material accumulates in the closed loop. Much evidence has been submitted to show that this loop poison causes the intoxication observed after producing a closed intestinal loop. Sufficient evidence has been presented to prove that the essential poison is present in these closed intestinal loops, and usually in concentrated form.

"Chemical study of the contents of closed intestinal loops shows that a single substance or group of substances possesses toxic properties. This resists autolysis and pancreatic and ereptic digestion. It is thrown out of solution by five volumes of alcohol or by half-saturation with ammonium sulphate. It is readily soluble in water and is not injured by boiling. It is not removed by dialysis. The method of isolation excludes practically all substances except primary proteoses. The characteristic resistance to digestive enzymes suggests a hetero-proteose.

"Proteose intoxication in dogs gives a picture identical with intestinal loop fluid; early salivation and vomiting, followed by diarrhea and prostration, fall in temperature and blood-pressure, and finally death in collapse. Autopsy shows essentially a splanchnic paralysis and remarkable engorgement of liver and spleen, but especially of the mucosa of the duodenum and small intestine. The blood shows great concentration due to loss of fluid and may remain incoagulable because of an excess production of antithrombin.

"Proteoses escaping from the blood are excreted in the urine. This toxic proteose concerned in intestinal obstruction has not yet been isolated in the urine, but may be excreted by the kidneys. This probably explains the clinical improvement and lessened intoxication noted after transfusion.

"Experimental evidence points to a primary proteose as the essential poison concerned in the intoxication of closed intestinal loops and intestinal obstruction." (Whipple, Rodenbaugh and Kilgore, *Journal Experimental Medicine*, 1916, xxiii, 123.)

Intestinal Digestion in Man after Excision of Large Portion of Lower Small Intestine. Gurévich¹ has been studying the extent of assimilation of alimentary substances in a man who had had 159 cm. of ileum removed. He found that only the carbohydrates are normally assimilated, nitrogen and fats very poorly. Instead of the 12.1 per cent., which is the normal rate for unassimilated nitrogen, there was 48.15 per cent. The tests were carried out seven months after the operation, during which time the carbohydrate metabolism had become normal, that of albumin and of fats was still deficient, but the patient was gaining in weight and was cheerful, though he still had persistent diarrhea.

¹ Abstract Journal of American Medical Association, 1915, lxx, 2128.

Appendicitis. **NEW SIGN OF APPENDICITIS.** Rutkevich¹ says that chronic appendicitis frequently occurs, runs its course under the form of various gastric and intestinal diseases, which are usually misinterpreted as some functional nervous disorder. During one year he encountered 76 cases of chronic appendicitis, all in women. In 60, an operation was done; 16 refused an operation. The disease usually occurred between the ages of 16 and 35, and in more than half of the cases it lasted two or three years. In 49 cases there was no history of previous attacks, which, however, might have been overlooked, if not very severe. Only 27 patients had a history of previous pain, usually in the right iliac region, radiating to the thigh, lumbar region, liver, etc. The pain was also located in some on the left side in the epigastric region, and in many cases was independent of the time of eating. Constipation was present in only 31 cases. McBurney's point was tender in 21 of 50 operative cases, and in 22 it was found painless. The temperature was found normal in 28 of the 76 patients, and Rovsing's sign was negative in all. Leukocytosis was found but once in 33 patients.

There are, therefore, no pathognomonic signs of chronic appendicitis. Palpation is the only reliable method. The appendix could be felt in 68 per cent., and in 88 per cent. it proved to be painful, and simultaneous pain was frequently noted at the points in the upper abdomen. Unfortunately, the appendix cannot always be palpated.

Rutkevich recommends a new method of exploration by adduction of the cecum. The flexed fingers of the right hand are worked between the external wall of the cecum and the abdominal wall, then, by extending the fingers, the examiner tries to push the cecum toward the median line of the abdomen. In cases of chronic appendicitis, this will cause pain. In all of the cases (76) this sign was positive, and was confirmed by operation. The pain can be explained by adhesions or by appendicitis. This sign in combination with palpation of the ileum (its sensitiveness or absence of pain) helps to differentiate appendicitis from diseases of the adnexa in the pelvis (salpingitis, oöphoritis, etc.).

BLUMBERG'S SIGN. The so-called Blumberg's sign is pain in the region of the appendix, following rapid removal of the hand after it has been applied to the spot to induce pressure. Nikolaiell² denies that it is a specific sign. He had been using this sign long before Blumberg, and found it not only in appendicitis but in every case of peritoneal irritation, whatever its cause. Thus he found it in perforative peritonitis, gastric or duodenal ulcer, in cholecystitis, typhoidal ulcers, etc. He usually examines each of the four quadrants of the abdomen. He gives the history of 5 of 340 cases in which he studied this sign. It is especially pronounced during the first 24 or 48 hours, being thus one of the earliest,

¹ Abstract Journal of American Medical Association, 1915, lxy, 987.

² Ibid., 1916, lxvi, 464.

and therefore one of the most valuable signs of acute involvement of the peritoneum by any of the above-mentioned diseases. In chronic peritonitis, for instance, tuberculous peritonitis, the sign is absent.

Occult Blood. Wolff¹ gives the detailed history of the study of occult gastro-intestinal hemorrhage to date, and emphasizes the diagnostic importance of positive findings, provided no meat had been eaten for the few days preceding. He emphasizes, further, the marked tendency of a solitary gastric ulcer to heal, which renders persistent occult hemorrhage so significant. He also comments on the necessity for strict regulation of the diet after operation on the digestive tract. He regards testing for occult blood as an indispensable routine procedure in all dubious stomach cases. In his own practice recently the positive, and also the negative, findings in a number of cases gave the clue to the real source of the trouble, confirmed by the later course of the cases. The value of the test was shown particularly in a case of severe anemia, with hemoglobin below 50, but no symptoms on the part of the digestive tract except occult bleeding. In another case there was intense cardialgia, and gastric ulcer was assumed, but no benefit followed treatment on this basis, and no occult hemorrhage could be detected. On this negative finding, treatment for syphilis was instituted and prompt recovery followed. In another case, anemia and nervous symptoms on the part of the stomach were assumed at first to be a recurrence of a gastric ulcer which had been successfully treated ten years before. The constantly negative tests for occult hemorrhage apparently excluded gastro-intestinal trouble, and under the general tonic measures health was soon regained. In a case of chronic hyperacidity, with pains, vomiting, and emaciation, the absence of occult bleeding excluded cancer, and no trace of malignant disease was found at necropsy. In gastric ulcer cases, the improvement under treatment could be followed in the subsidence of the occult hemorrhages. Occult blood also revealed, in some cases, the presence of malignant disease in the stomach before there was any tumor or debility, and in many dubious cases turned the scale one way or the other, and always reliably, according to Wolff's experience to date.

OCCULT BLOOD WITH GASTRIC CANCER. Emmert² found occult blood in the stool or stomach content in all but 1 of 21 cases of what proved to be gastric cancer. This symptom is not only exceptionally constant, but is present when the patient first applies to the physician, as a rule. In one of his cases there had been symptoms for only four weeks, and operation showed the cancer merely as a thickened patch not as large as a silver quarter. In one case of gall-stone trouble, the occult blood revealed the presence of the concomitant gastric cancer. A negative response to the guaiac test renders malignant disease in the stomach or

¹ Abstract Journal of American Medical Association, 1915, lxxv, 2206.

² *Ibid.*, 1916, lxxvi, 1360.

bowel extremely improbable, he declares. When a gastric ulcer is developing cancer, the regular presence of occult blood gives the clue to what is going on. Even when the stomach is opened, it is not always possible to distinguish between simple ulcer and cancer. He advises the application of the guaiac test at intervals, even with certain ulcer, as thus any tendency to cancerous degeneration would be promptly recognized. He examined the stomach content for occult blood in 261 cases, aside from his ulcer patients. The findings were constantly negative except in 10 cases. In 6 of these the response was positive only at the first application of the test, and the diet was responsible for it in some of these. No explanation for the positive response could be found in the 4 others out of the total 261 tested.

TESTS FOR OCCULT BLOOD. Salvin¹ has been investigating the various technics for detection of invisible blood in the stomach content and feces. The benzidin technic and Ganassini's eosin reaction gave the clearest responses, and this promptly, while they are sufficiently sensitive (in proportion down to 1 per 15,000) for all practical purposes. He warns that only the findings in the first thirty minutes are reliable. In Ganassini's method, 0.5 c.c. of crystallized eosin are dissolved in 100 c.c. of absolute alcohol. In another vessel are 2.5 c.c. of potassium hydrate dissolved in alcohol and 2 c.c. of distilled water. Then, in a third vessel, all the potash solution is mixed with 10 c.c. of the eosin solution, and the whole kept in boiling water for 8 to 10 minutes. It is then cooled, and a drop or two of alcohol are added to replace what has been lost by evaporation. When ready to use, 1 c.c. of 10 per cent. hydrogen peroxide is added to 5 c.c. of the reagent and the fluid to be examined is dropped slowly into the mixture. With a positive reaction, the blue tint veers to yellow or orange, with a greenish or yellow fluorescence. This reagent must be kept in a cool place and protected from the light. The hematin acts as a catalase, fixing the oxygen to the eosin, and thus enabling it to regain more or less its former tint which the potassium has changed to blue.

Roberts,² in order to overcome the necessity of making fresh benzidin solutions daily, and in order to obviate the danger of using deteriorated hydrogen peroxide, has devised an extremely satisfactory benzidin tablet. The triturate is composed of one part benzidin to 20 parts sodium perborate triturated with great care and made up into a 5-grain tablet. The specimen to be tested is placed in a small saucer, in sufficient quantity to wet the tablet thoroughly but not to immerse it. A drop or two of glacial acetic acid in the tablet, if blood be present, gives rise to a more or less immediate change in the tablet to a greenish blue. The delicacy is slightly less than the usual test, but is delicate enough for all practical purposes.

¹ Abstract Journal of American Medical Association, 1916, lxvi, 463.

² Ibid., 1915, lxv, 244.

This test of Roberts's is decidedly more simple than the usual test. There is one objection which may be made, however, and that is that animal, as well as vegetable, ferments give a positive reaction with benzidin, and unless these ferments are rendered inert, which may be readily brought about by boiling, sources of error are liable to occur. In Robert's test, no provision is made to guard against ferment action in the stools or gastric contents.

Carbohydrate Indigestion. Carbohydrate indigestion is a functional disturbance, the symptoms arising as a result of fermentation, with the production of carbon dioxide, methane and volatile fatty acids. The exact cause is unknown, but several hypotheses are advanced by Tileston:¹ (a) Hyperacidity, by interfering with the action of the salivary diastase, (b) the presence of undigested or partially digested starch in the large intestine, together with the action of microorganisms; (c) defective digestion of the cellulose envelope of the starch cells.

The symptoms are usually those due to distention with gas. There is a sense of fulness and discomfort coming on several hours after meals, accompanied by flatulence. When there are higher degrees of tympanities, there is colicky abdominal pain, relieved by the expulsion of gas per rectum. The pain may be general or may be local in any area of the abdomen. When there are adhesions, pain is more likely to occur. When there is irritation of the bowel through the acid products of fermentation, diarrhea is seen, the so-called "fermentative dyspepsia" of Schmidt. There is also gastric fermentation, relieved by belching.

The diagnosis must be made only after the causes of tympanities have been considered; (1) Increased gas production, (2) mechanical obstruction of the bowel, (3) paralytic ileus, (4) deficient absorption of gas from the bowel. After the exclusion of the sources of tympanities, that due to increase of gas production remains. The stool examination is important, and when the reaction is acid and there are undigested starch granules (iodine test) much evidence has been obtained. Schmidt's fermentation test is seldom indispensable.

The treatment is mainly dietetic. Starches must be reduced and certain articles must be excluded, namely, white and sweet potatoes, cabbage, beans, (except string beans), and chestnuts. When the case is obstinate, a diet consisting of eggs, meat, fish, bouillon, butter, cream may have to be prescribed. After a few days, sugar, cream of wheat, toast or zwieback, macaroni, and rice in the order named, may be cautiously added, one at a time. It is best to taboo potatoes for a long time. Of drugs which are of doubtful value of themselves, the various salicylate preparations and betanaphthol may be used. Diastatic preparations are rarely of service.

Wolff² expatiates on the necessity for exact differentiation of the factor

¹ Journal of American Medical Association, 1915, lxxv, 2214.

² Ibid., 1916, lxxvii, 158.

inducing abnormal conditions in the intestines; the treatment required for one may be the exact opposite of what is required for another. He emphasizes the importance of ascertaining the way in which cellulose is digested as the guide to treatment. When stomach and bowel are functioning to excess, cellulose is digested so completely that not enough residue is left to keep the bowels moving properly, and chronic constipation is liable to result. When stomach and bowels are functioning adequately, the cellulose does not get digested enough, and the carbohydrates, which are enclosed in the cellulose, ferment. Certain persons seem to have a limit for digesting cellulose and above this limit they cannot go. The less constitutional the limitation, the easier it is to influence by diet and training. When the individual limit at the time is surpassed, the stools soon present the fermentation type, with diarrhea and symptoms of dyspepsia and neurasthenia.

"Gastrogenous" and "nervous" diarrhea do not present the fermentation type of stools. The fermentation type is semifluid, or fluid, light yellow, foamy and full of gas, highly offensive, with an odor of acetic and butyric acid. When mixed with water, the naked eye readily recognizes the remains of undigested potatoes as round lumps like grains of sago. In contrast to this, as a rule, there is very little mucus, and the microscope shows that there is remarkably little muscle residue or soaps. Wolff has encountered, in the last two years, 10 cases of this fermentative diarrhea from inability of the intestines to digest cellulose. In some there was subacidity of the stomach, in others superacidity, and in some the stomach seemed to be functioning normally. In treatment, the intestines must not be burdened with cellulose and substances that ferment readily. Farinaceous food of all kinds must be used very sparingly, and these restrictions must be kept up for a long time. He advises refraining from everything of the kind for a few days, living on well-cooked meat, fish, and gelatine preparations, eggs, bouillon, milk, tea, light wine, and a little more sugar than usual. With this as the standard diet, variety can be obtained with a little honey, infants' artificially dextrinated foods, fine wheat flour dishes and tapioca. Later, toast and biscuits may be allowed; the purées of fresh young green vegetables, stewed fruits and preserves. The diet is thus regulated by the proportion of cellulose and easy digestibility, guided by the character of the stools. The tolerance for cellulose may increase, but potatoes, uncooked vegetables, and uncooked fruits must be avoided for a long time or relapses may follow. He was impressed with the benefit derived in cases of deficient gastric secretion from the systematic administration of hydrochloric acid and pepsin. This aids, not only in gastric digestion, but in the digestion going on in the bowels. Even better results were obtained by supplementing this with pancreas ferment, in some cases. A mild antiseptic for the bowels was also found useful, guaiacol carbonate plus nux vomica in small doses (0.05 gram and 0.1 gram respectively). He

generally concludes the treatment with a course of natural iron mineral waters, combined with some saline mineral water. This aids in toning up the general health and combating the anemia and nervousness which often accompany this type of "intestinal dyspepsia."

Gastrogenous Diarrhea. Dziembowski¹ discusses the role of hydrochloric acid in digestion, and the reasons why lack of an adequate amount of it is liable to entail intestinal dyspepsia. He thinks there can be no doubt that the hydrochloric acid has a certain disinfecting action on the food, destroying fermentation-producing germs, which otherwise set up fermentation farther along in the alimentary canal. The lack of hydrochloric acid also does away with the reflex closure of the pylorus. We know that the pylorus closes up when the acid comes in contact with the duodenal mucosa. When this does not occur, the pylorus gapes continuously, and, in time, atony results. Conditions thus being the extreme reverse from the pylorospasm with hyperacidity with its resulting constipation. Still another factor in the gastrogenous diarrhea is the mechanical irritation of the bowel lining from the undigested particles of food emerging from the stomach. This mechanical irritation extends also to the musculature of the bowel wall, and it responds to this irritation with augmented peristalsis. The bowel content is thus passed with abnormal haste. There may be then abdominal pain and diarrhetic stools after nearly every meal, and undigested particles of food are seen in the feces. We know pepsin acts only in an acid medium, and that albumin cannot be digested with hydrochloric acid. Even starch grains require hydrochloric acid to release them from their albuminous coating. The stools with gastrogenous diarrhea show pronounced cretatorrhea and moderate steatorrhea. The latter differs from that in pancreatic disease, in that no fat needles or fat crystals are evident, only lumps of fat. Gastrogenous diarrhea is liable to develop with achylia from any cause, and he discusses in detail the various causes which have been observed. With derangement of the vegetative nervous system, anacidity and hyperacidity may alternate, entailing periods of diarrhea and constipation in turn.

In the treatment, we must bear in mind that the bowel mucosa is probably irritated and hence food liable to aggravate this irritation must be avoided. Dziembowski approves of giving aromatic and bitter substances to stimulate gastric secretion, but not meat and spices until the bowel has been restored to normal by local medication. In conclusion, it is recalled that unsuspected syphilis may be at the bottom of the whole trouble. Many cases are on record when treatment of syphilis soon brought about a complete cure after failure of all other measures.

It is probably not fair to take exception to an article when only an

¹ Abstract Journal of American Medical Association, 1916, lxvi, 1279.

abstract is read, but it seems that absence of hydrochloric acid is not the true cause of this form of diarrhea. At least, many cases are seen in which a pronounced achylia is accompanied by constipation of most pronounced degree, and I have at the present time many cases of this nature under my care. Again, exception may be taken to the recommendation that bitter tonics be prescribed, inasmuch as Carlson has definitely shown how really inefficacious they are. He says their main value lies in being a "handmaid to psychology," and it is about true that if proper diet and hygiene do not augment hunger and appetite, the chances are that tonics will contribute nothing to bring about this end.

Effect of Opium Derivatives on the Gastro-intestinal Tract of Man. Last year (page 91) I called attention to Pancoast's preliminary work on *x*-ray studies on a patient who had received a hypodermic injection of morphine the evening prior to examination. An hour-glass stomach was found, and also a striking retardation of the motility of the small intestine. When freed from the influence of morphine, no such abnormalities were observed. Pancoast and Hopkins² have continued this work of Pancoast's and now make a preliminary report. The authors anticipate criticism of the work, which they realize is far from conclusive. The surprising result was the lack of any degree of uniformity in the effects produced in different individuals. In no one of their 11 cases were the unusual phenomena repeated which were observed in the case reported by Pancoast (see above). Of much interest was the appearance of anti-peristalsis in three cases. As a rule, morphine was found to cause decreased motility in the small intestine, apparently as a result of a lack of propulsion and not of spasm. When marked, it is most noticeable in the upper small bowel. The effect on the large bowel is very variable, and probably of little consequence, and it makes little difference whether the opium is given by mouth or hypodermically.

Enteroliths. Two cases are reported by Pfahler and Stamm,³ the clinical symptoms being pain at the site of the enterolith, nausea, vomiting and diarrhea. The condition must be very rare, as only 10 cases could be found reported in the literature. The authors do not mean by enteroliths, the small sand-like particles so frequently found by those who make it a practice to examine the stools as a matter of routine, but the masses which may be recognized by the *x*-ray. They should always be suspected when there is a movable mass in the abdomen, and when opaque bodies are found in the appendiceal region during the course of a Röntgen examination of the ureters. Operation does not seem to be indicated, as the use of glycerin enemata and massage usually causes their rejection.

¹ PROGRESSIVE MEDICINE, 1915, p. 30.

² Journal of American Medical Association, 1915, lxx, 2220.

³ Surgery, Gynecology and Obstetrics, 1915, xxi, 14.

Diet in Chronic Disease of the Intestine. Borgbjaerg¹ emphasizes the importance of the diet as a factor in the successful management of chronic intestinal disturbance. Schmidt and Strasburger have demonstrated the nature of dyspepsia from intestinal fermentation and the means to bring it under control. Borgbjaerg here discusses colitis, saying that the primary cause is often to be found outside of the colon. Cure of this is followed by the healing of the bowel trouble. The same applies, only in higher degree, to extreme constipation. It is often merely one symptom from a gastric ulcer, appendicitis or gall-stone trouble, and subsides with relief from the primary trouble, especially when proper dietetic treatment is instituted. Even when it is primary, there are many factors which have to be considered. He advocates extensive use of milk in the diet with chronic bowel trouble, especially colitis, cautiously increasing the doses and examining whether it tends to induce diarrhea or constipation, or neither, in the individual case. The idea that milk is poison for the bowels, he says, is a mistake. It is a good and nourishing food, and inability to assimilate it properly may be due to absence of the normal bowel content of lactase. It has been observed that in mammal animals lactase was produced only so long as milk-sugar was obtainable in the diet, and *that*, only during the suckling period. The physician too often depends merely on the patient's statements as to constipation, etc., and orders a diet rich in waste which is certain to aggravate abnormal conditions already installed.

Rectal Feeding. Begtrup² presents evidence to show that milk and eggs in nutrient enemas cannot be absorbed and eliminated, theoretically speaking. Native albumins are not absorbed as such, coagulable albumin being scarcely able to pass through an animal membrane, while there are no active digestive ferments in the lower bowel. Hence, Begtrup experimented with further digested substances, meat amino-acids, and milk amino-acids, with sugar, a large proportion of which seems to be absorbed. Sugar irritates the intestinal mucosa so that the amount has to be kept low. The patients had all had hemorrhage recently from the stomach and bowel, and had been given nothing by the mouth for from two to seven days. Then the nutrient enemas were commenced and the metabolic findings systematically tabulated. Two or three nutrient enemas were given each day, diluted with water up to 200 to 250 c.c., and introduced in the bowel as high as possible. The tabulated metabolic findings show a decided increase in the amount of nitrogen eliminated in the urine during the amino-acid enema period.

¹ Abstract Journal of American Medical Association, 1916, lxvi, 318.

² *Ibid.*, 1062.

DISEASES OF THE GALL-BLADDER AND LIVER.

Contractile Movements of the Gall-bladder. Okada¹ in this paper records his researches on the contractile movement of the gall-bladder during digestion. He found that spontaneous contractions occur about two to five times per minute, which are, however, not all characteristic. At times, none is seen, even after an hour or more of observation.

He recorded the movement of the gall-bladder after a meal of meat, and found that there was a great increase in rhythmic contraction at the height of digestion. The frequency of the rhythm is variable, sometimes the recur at the rate of one to three per minute, sometimes the contracted state continues a long time with a series of short interruptions and relaxations.

Acid and other liquids caused some increase in contractions, but water causes a very insignificant increase. Chloral hydrate, an efficacious cholagogue, produces a quite regular rhythm.

Reaction of Bile. Okada² measures the values of H-ion concentration of the bile from the gall-bladder in a series of animals, and found that it may be acid, neutral or alkaline. This invariably is found in different animals of the same species. Okada discovered that the bile from the gall-bladder and from the liver had a different reaction, the former being more variable and always inclining to the acid side, while the latter is alkaline. During digestion and during fasting, the reaction varies, but is not dependent on the various kinds of foods. The liver bile during digestion has a reaction corresponding to that of pancreatic and intestinal juices, and with the optimal point for trypsin pancreatic lipase and erepsin.

Bile-pigment Metabolism. The generally accepted theory covering the life history of the bile pigments, is that degeneration of red cells frees hemoglobin, which is brought to the liver and there changes to bile pigments which are excreted as waste products into the intestine. Here the bile pigments are reduced to urobilin or stercobilin, some of which may be absorbed and returned to the liver and again thrown out in the bile or destroyed. Some of the urobilin may escape the liver and appear in the urine, especially when the liver is not functioning normally. Hooper and Whipple³ believe that the bile pigment secretions can be influenced at will by modification of the diet, indicating that the liver has a constructive function in forming bile pigments as well as the accepted eliminative function.

In their first paper (*rid ob.*) Hooper and Whipple confine themselves to questions of technic, and the study of bile-pigment excretion under uniform conditions. The normal flow of bile is very variable, as shown by

¹ Journal of Physiology, 1915, 1, 42.

² Ibid., p. 114.

³ American Journal of Physiology, 1916, xl, 332.

Stadelmann, a matter which cannot at present be explained. All things being equal, the bile-pigment excretion may form a pretty uniform curve, the daily amount being one milligram per pound body weight per six hours. In their second paper¹ the authors show that a diet rich in carbohydrates or sugar, administered by mouth or intravenously, will increase the secretion of bile pigments. This curious action of carbohydrates upon bile-pigment formation overthrows the long-accepted theory that bile pigment is found only as a result of the disintegration of erythrocytes. A convincing explanation of this phenomenon is not brought forward, the authors requiring more experimental data before committing themselves.

On the other hand, a mixed diet is associated with a fairly constant mean bile-pigment elimination, but a change to a meat diet depresses the average bile-pigment elimination.

Extrahepatic Formation of Bile Pigment. Hooper and Whipple three years ago were able to show that bile pigment would be formed from hemoglobin without the agency of the liver. Since that time other experimenters have arrived at the same conclusion, and last year I described in *PROGRESSIVE MEDICINE*, December, p. 115, some work of Van den Bergh and Snapper showing conclusively that bilirubin in their case had been formed in the spleen. Hooper and Whipple now demonstrate the fact that the mesothelium of the pleural and peritoneal cavities can transform hemoglobin into bile pigment. This is a new phase of the problem which has not heretofore been described, and is a further proof that participation of the liver in bile-pigment formation is not obligatory.

Later experimental work by Van den Bergh and Snapper² has definitely proven that the spleen at times may assume the function of bile-pigment manufacture.

The Secretion of Bile. Okada³ has found very little difference in the effect on the secretion of bile during the first six or seven hours between the diets of bread, butter and meat, if these substances be administered in quantities of corresponding caloric value. Starvation tends to diminish the secretion of bile and the excitatory effect of feeding on the liver cells. The following substances introduced into the stomach cause an increased secretion of bile:

- Raw white of eggs.
- Boiled egg white.
- Fat and oil.
- Soap solution.
- Acid (very marked).
- Witte's Pepton.
- Liebig's extract of meat.
- Bile salts or bile.

¹ American Journal of Physiology, 1916, xl, 349.

² Berl. klin. Woch., 1915, 1081.

³ Journal of Physiology, 1915, xlix, 452.

Secretion injected into the blood cause secretion of a dilute bile.

The following substances eaten, or introduced into the stomach, produce little or no effect:

Pure cane-sugar.

Cakes of baked starch and sugar.

Water.

Solution of sodium bicarbonate.

Certain drugs increase the flow of bile, such as sodium salicylate (markedly), salol (slightly), chloral hydrate (markedly), cream of tartar, alcohol (in large quantities). Calomel is without effect.

Does the Cholesterol in the Food Influence the Biliary Cholesterol Excretion? According to Naumyn and the pupils of his school, the variety of food eaten exercised no influence on the amount of cholesterol excreted in the bile, and based on this was erected the belief that cholesterol was but a decomposition product of gall-bladder epithelium and was in no sense a true product of metabolism. The writer¹ was the first to show the fallacy of this theory, and, under Hofmeister's direction, was able to demonstrate that food did influence the composition of the bile. A diet rich in protein increased not only the cholesterol but also the bile acids, and a similar result was obtained when calves' brains or erythrocytes, both containing large quantities of cholesterol, were ingested. If, on the other hand, cholesterol was introduced into the circulation directly, neither the cholesterol in the bile nor the bile acids were at all increased. It would seem from this that the protein-rich food stimulated the liver to activity, and increased the quantity of its secretory products.

Later work has substantiated this work, notably that of Kosumoto, Bacmeister and Ignatowski and Monossohn. Nevertheless, there remains a gap in all this work, to wit: Is the cholesterol, which is taken with the food, excreted in the bile?

D'Amato² has made this question a subject of considerable study, and found an absolute increase in the amount of bile excreted after giving a diet rich in cholesterol, as compared with the amount determined on a carbohydrate diet. This is in accord with what I found in the bile, but the question suggests itself, If 5 or 6 grams of cholesterol are fed to an animal, and but 1 or 2 mg. are found in the bile, what has become of the remainder? Martiri believes that in an animal with a biliary fistula there is a continuous loss of cholesterol and the organs become "a-cholesterolized," if I may coin this word. When a large amount of cholesterol is ingested, therefore, the greedy organs seize upon it and retain it. This is hardly correct, for, as d'Amato says, the amount of cholesterol excreted by a dog is only a few centigrams and it would take at least three or four months for an animal to lose a gram.

¹ Goodman, Beitr. z. chem. Physiol. und Pathol., 1907, p. 9.

² Biochem. Zeitsch., 1915, lxi, 217.

D'Amato prefers to believe that the bile is not the only method of elimination for cholesterol received from diet, and again, he believes that the Naunyn school is in error when it claims no relation between food and cholesterol output. He believes it is incorrect to assert that the ingested cholesterol is converted into bile acids and is excreted as such.

Clinical Studies of the Bile. Medak and Pribram¹ have, by means of the duodenal tube, been able to secure bile, which, in many pathological cases, they have examined for pigment, cholesterol, and bile acids. Bile acids have furnished very little which is of interest clinically, although the importance of this study must still remain an open question.

The patients were selected so as to have a group which promised to furnish interesting results. The diseases comprised anemia, gall-bladder disease, nephritis, arteriosclerosis, cirrhosis, cardiac cases, pregnancy and tumors. The study of bile pigment is particularly important and the authors believe that a marked increase is a definite indication of splenectomy when anemia is progressing. Studies made after splenectomy show that by the operation the bile pigment is brought to normal, and coincidentally there is an increase in the number of red blood cells.

Urobilin in duodenal juice speaks in a way for infection of the biliary tract, inasmuch as there is no urobilin when there is no infection. However, this diagnostic sign is qualified to a certain extent, for hepatic insufficiency is accompanied by urobilin.

Hypercholesterolemia, as seen in cholelithiasis, nephritis, cirrhosis, diabetes, is associated with hypocholesterocholia. After splenectomy, blood cholesterol increases, while bile cholesterol falls. In pregnancy the bile cholesterol is markedly diminished until, at the end of the ninth month, only traces are seen.

This work of Medak and Pribram, while not conclusive, is nevertheless suggestive. It is impossible to obtain quantitative estimates of the twenty-four-hour duodenal juice, but the authors appreciate this as well as their critics, and have made due allowance for similar objections.

Duodenal Tube in Gall-bladder Disease. Einhorn² has also made use of the duodenal tube in studying gall-bladder disease, relying mostly on the macroscopic appearance of the bile. The patient is given the duodenal tube either at night before retiring, or at 5 A.M. He takes it with a glassful of water. About 8 or 10 A.M. the patient is then examined in the fasting condition, and the contents aspirated. In the majority of cases in which turbid bile is found in the duodenum, cholecystitis, with gall-stones, is encountered. Turbid bile may, however,

¹ Berl. klin. Wochenschr., 1915, 706, 740.

² Journal of American Medical Association, 1916, lxvi, 1908.

exist without gall-bladder disease, when the liver itself is seriously diseased, or when there is stricture of the duodenum below the papilla of Vater. On the other hand, even with biliary calculi, clear bile may be obtained. In these cases, no bile enters the duodenum, because the gall-bladder is filled with calculi, or else the gall-bladder is not inflamed, notwithstanding the presence of the stones. A clear golden bile speaks well for the integrity of the gall-bladder or liver, while a turbid, greenish, or dark brown-looking bile, perhaps mixed with mucus, speaks for a diseased state of either the gall-bladder or liver, or both. In gall-bladder affections the bile is liable to change in character, whereas in permanent disease of the liver, the appearance is stabile. Einhorn warns that the diagnosis of cholelithiasis cannot be made from the appearance of the bile alone, but clinical signs must be taken in conjunction.

Microscopic Study of Bile in Liver Disease. McNeil¹ recommends the examination of fresh bile which he obtains by the duodenal tube after a fast of twelve hours. The examination must be made immediately since only a few moments are required for the complete destruction of the important cellular elements or for serious mutilation of the pancreatic ferments. The fresh contents are placed on a slide and studied first with a low-power lens and then details are studied with the high power (not oil immersion). Normally, the duodenal contents contain cellular elements with the exception of an occasional squamous cell from the mouth or esophagus.

Abnormal findings are: (1) bile-stained, granular casts, occasionally containing a bile-stained cell, and suggesting casts of the finer bile passages; (2) bile-stained leukocytes, usually polymorphonuclear, occurring in groups, and associated with (3) a round oval, deeply bile-stained refractile cell, about double the size of the preceding and containing a round, small, eccentric nucleus. This cell is extremely fragile and soon disappears, to be replaced by deeply bile-stained and highly refractile masses; (4) columnar bile-stained epithelial cells apparently from the linings of the gall-bladder or bile ducts; (5) bacteria, yeasts, and protozoa; (6) mucus.

In certain diseases of the liver, particularly in atrophic cirrhosis, definite abnormal cellular elements are seen. These elements being of diagnostic importance in this disease and in acute cholecystitis. Abnormalities of the fresh bile are rarely found in other forms of hepatic disease (syphilis, chronic passive congestion, abscess, carcinoma). Duodenitis may be satisfactorily diagnosed and studied when examinations of fresh bile are made.

Gall-stones. **CALCIUM CONTENT OF THE BILE AND ITS RELATION TO THE FORMATION OF GALL-STONES.** Calcium is found in all gall-

¹ Journal of Laboratory and Clinical Medicine, 1916, 1, 594.

stones; in the cholesterol stones there is but little, in the other varieties there is more. It arises from the bile, and the next thought naturally is, that when there is a large amount of lime, calcium stones are formed, and when there is a higher percentage of cholesterol, cholesterol stones are produced. In inflammatory conditions of the biliary tract, and particularly when the contents of the gall-bladder become obstructed, calcium is said to be increased. This latter supposition, although not based on clinical experience, is founded on experimental work which has shown that when the common duct is obstructed, more calcium is seen the longer the obstruction has lasted.

Lichwitz and Boch¹ have attacked this problem anew, using as their material bile removed at the time of operation. Gall-bladder bile was employed, also liver bile. Accepting the figures of 85 to 352 mg. pro 1000 grams of bile as the normal amount of calcium, the authors failed to find any evidence that the lime content of the bile rises in inflammatory states of the biliary tract. On the other hand, a decrease was usually the rule. They found, however, when there were masses of mucus there was from four to five times as much calcium as in the bile itself, due to mechanical irritation of bilirubin-calcium.

In the course of his work on high titer agglutinating sera against cholera-like vibrios, Greig² found lesions of the gall-bladder, around which, as centers, calculi had been deposited. In other cases he suspects that the vibrios themselves had formed the center.

TREATMENT OF CHOLELITHIASIS. Boas³ relates that the war with its nervous strain, the changes it has brought about in the financial status, the food, and other conditions of living, has entailed many ailments not only among the troops, but also in the civilian population, such as never were encountered on the same extensive scale in times of peace. Chief among them, according to his experience, is gall-stone trouble. Cholelithiasis affects mostly women, and especially married women, and these are the ones who are hardest hit by the war, worrying for sons and husbands, the breaking up of the home, and, connected with this, the neglect of their own health, the high prices of provisions—these, and other circumstances, combine to prepare the soil for the development of gall-stones or fan a latent tendency to a flame. Cholelithiasis, he remarks, may thus be regarded as a war malady. Internal medicine has only a limited field in the management of cholelithiasis. To claim otherwise, he continues, is to reveal a childish misconception of the mechanism of gall-stone production.

The custom of giving morphine to arrest the attack goes directly counter to Nature's efforts to expel the foreign body. The pain can be relieved in other ways, by hot compresses, hot tea, etc., which

¹ Deut. med. Wochenschr., 1915, p. 1215.

² Indian Journal Med. Research, 1915, iii, 259.

³ Abstract Journal of American Medical Association, 1916, lxvi, 542.

reinforces Nature instead of neutralizing her efforts. If a sedative is absolutely necessary, use the smallest doses, and select chloroform, papaverine, or codeine, explaining to the patient that by abstaining from morphine, there is much better chance that the concrement may be expelled and not give cause for future attacks. Perhaps the reason why there are so few "successful attacks" nowadays is because morphine is given so freely.

Boas has for years derived great benefit from local blood-letting, scarifying the skin in the gall-bladder region and keeping up the bleeding with a suction bell. It is easy to draw considerable blood in this way. This is especially useful with acute gall-bladder trouble, or acute enlargement of the liver. It is astonishing to see the complete subsidence of all disturbances; the day after the blood-letting, the patients are able to go about their work as usual. He adds that when we consider the mechanical conditions, the assumption that measures to promote the flow of bile will wash away the stones or prevent the formation of new concretions, is as fantastic as the naïve idea that gall-stones in the body can be dissolved by chemical means.

A number of factors are known to help in eliciting gall-stone attacks, and avoidance of these factors tends to ward them off. Persons with gall-stone trouble almost invariably have a history of habitual constipation and functional disturbance in the stomach, usually achylia gastrica, or there may be hyperchlorhydria or sagging of the stomach and bowels. Undigested, or half-digested, food in the duodenum presses on and obstructs the common bile duct, or offers opportunity for immigration of microbes into the bile passages. The fact that the gall-stone attack occurs when the digestive tract is overloaded confirms this assumption. Gall-stone attacks never seem to occur with stenosis of the pylorus. The behavior of the stomach must receive more attention than hitherto in the management of cholelithiasis. Large meals, especially at night, should be strictly avoided. In short, he regards dietetic measures as the main element in treatment of cholelithiasis, small light meals at intervals of two or three hours, avoiding raw fruit, salads, black bread, and pickles. As cholelithiasis is such an essentially chronic affection, treatment must be continued to correspond. Of great value are the various elements of spa treatment, rest, dieting, regular meals, baths, and outdoor exercise, besides drinking the mineral waters, but he advises a six or twelve months' stay. This offers the most favorable chances for keeping the gall-stone trouble latent.

A stone impacted in the common bile duct is dangerous mainly on account of the cholemia, with its depressing influence on the general health, and the uncontrollable pruritus. He has never known of an instance of a gall-stone being forced out of its nook by medical measures alone. Hence, he advocates operative measures here, without wasting time on others.

But medical measures are generally effectual in simple catarrhal or purulent gall-bladder disease; all that is required is cautious dieting, ice to the liver, and small doses of narcotics. When the inflammation in the bile passage or gall-bladder is very severe, with fever and chills, the systematic administration of calomel, 0.1 gram three times a day, kept up for at least four weeks, may save the patient an operation. The Russians, who introduced this calomel treatment, give large doses, up to 0.5 gram several times a day. Boas has had the treatment fail in a few cases, but as a rule it is effectual. After the chills and fever are arrested by it, he resumes the calomel again if the trouble flares up again. Conditions are more favorable for retrogression when the disease process is in the gall-bladder alone. He has never been successful with medical measures in chronic cholelithiasis or in the disturbances from adhesions to that organ. Palliative treatment does little good and operative relief is called for, especially when the patient has not the time or means for rest cures, etc. As regard the rare occurrence of gall-stone trouble after an operation, Boas remarks that it is never comparable to the primary trouble, and usually yields to a course of spa treatment. The disturbance may be due to recurrence of stones or to postoperative adhesions (see below for discussion of this).

RECURRENCE OF GALL-STONES AFTER CHOLECYSTECTOMY. Kadian¹ reports in detail a case of cholelithiasis operated upon with removal of the gall-bladder. Six years later the patient returned with new symptoms indicating cholelithiasis. Operation was advised, and at the second operation a new-formed gall-bladder was found continuous with the common duct. The latter contained about ten cholesterol stones. Kadian gives a review of 28 cases, somewhat similar, which he gathered from the literature. In his case, a small stone must have been, he thinks, left in the common bile duct, which must have gradually increased in size because of deposits of bilirubin salts. The origin of the gall-stones he ascribes to the liver itself. Some relapses, with new formation of gall-stones, are exceedingly rare. To prevent recurrence, the operation must include not only the removal of the gall-bladder and the stones within, but opening up of the common bile duct and removal of all concretions. The cystic duct must be ligated as low as possible to avoid formation of a diverticulum to form a new gall-bladder. No ligatures, sutures or gauze thread should be left in the duct.

This recalls cases quoted in *PROGRESSIVE MEDICINE* last year, page 118. Stanton contended that the majority of similar cases are ascribed to the failure to make a thorough search for calculi, other than in the gall-bladder, and Lameris also makes this contention. Scrupulous care in operating, so that no foreign body (threads, unabsorbable suture material) is left, is most necessary, as these may form a nidus for calculi.

¹ *Journal of American Medical Association*, 1916, lxvi, 1666. Abstract.

Stanton claims that "the reformation of gall-stones is so rarely observed as to constitute almost a negligible factor in gall-bladder surgery."

Carcinoma of the Gall-bladder. In the beginning of the disease the symptomatology is protean, in one case the course is so mild that it may be considered a simple gastric catarrh, in another instance it resembles the severest form of cholelithiasis. This variation depends upon the location of the tumor, upon the presence of calculi or inflammation. Just as a stone, as such, without inflammation causes but little discomfort, so will carcinoma, if confined to the interior of the gall-bladder, be symptomless. A nodule of cancer the size of a hazel nut behaves no differently from a cholesterol stone in sterile bile. Even when the wall is penetrated and the serosa invaded, there may be no suspicion of the neoplasm, nor may there be any when the liver is involved.

The case is different when the tumor is in the neck of the gall-bladder, for in this event there is a rapid closure of the cystic duct. If calculi are coexistent, infection is almost sure to be present, and when the cystic duct becomes closed, acute cholelithiasis is the rule. If there are no calculi and if the gall is sterile, no prominent subjective symptoms may present themselves.

Kehr¹ reports in detail several instances of the insidious onset of carcinoma, and raises the question of how can the diagnosis of malignancy be made with any degree of accuracy? The history is rarely of great value. Jaundice and colic are but manifestations of cholelithiasis. Pain is not a symptom of cancer but an expression of cholelithiasis and of empyema. Percussion and palpation are also of little value. A large, painless gall-bladder tumor indicates hydrops of the bladder; if painful, empyema may be diagnosed, but if behind the cause of either, a stone or carcinoma is hidden, one can but guess, he is never certain. If the tumor is nodulated, suspicions of cancer should be entertained, but Kehr warns one to be on his guard lest a thickened mesentery be the cause of the irregular feel. The *x*-ray is of no assistance. The various serodiagnostic tests promise but little. The surest means of diagnosis is inspection of the gall-bladder after laparotomy, yet even this apparent certain way is by no means positive, since a carcinomatous gall-bladder, externally inspected, is no different from an inflamed structure. An ulcer looks like a malignant neoplasm. Only microscopic study furnishes the correct and final diagnosis.

Kehr believes in Riegel's dictum "that if a patient wishes to avoid carcinoma he must have his gall-bladder, together with all calculi, removed." He recommends, therefore, an early operation for any chronic infection of the gall-bladder, a somewhat paradoxical and Hibernian remark. Of 350 operations for gall-bladder carcinoma, only

¹ Berl. klin. Wochenschr., 1915, p. 1159.

8 have recovered, *i. e.*, 2.3 per cent., a shocking result when the mortality of gall-bladder operations for causes other than malignancy is but 1 or 2 per cent. The reason for this is, alas, too plain; the patients come too late to operation because of the uncertainty of the diagnosis, but also because chronic cholecystitis is not offered early surgical aid.

Phenoltetrachlorphthalein Test for Liver Function. McLester and Frazier¹ have made use of the phenoltetrachlorphthalein method of Rowntree, Hurwitz and Bloomfield. An accurately measured quantity of a freshly prepared solution of phenoltetrachlorphthalein greatly diluted, was given intravenously; 30 to 45 per cent. of this dye is normally excreted by the liver and can be recovered in the feces (forty-eight-hour collection). After the proper diluting, shaking and clarifying of the feces, the phthalein is estimated in a colorimeter. (Details of the test will be found in *PROGRESSIVE MEDICINE*, December, 1914, page 88.) The authors arrange their 100 cases in three groups: Group I comprises primary liver disease; Group II, myocardial insufficiency with subsequent liver involvement; Group III includes miscellaneous cases.

Five of the five cirrhosis cases had a normal output of the dye. The cases in Group II present bizarre results, certain of the cases showing marked liver engorgement and low phthalein output would encourage one to believe that here one has a means of measuring liver injury. On the other hand, some of the most extreme cases of this group gave a normal amount of phenoltetrachlorphthalein in the feces. Taking this group as a whole, McLester and Frazier find no relationship between liver engorgement and phenoltetrachlorphthalein output. In Group III were seen wide variations for which no explanation is offered. The writers conclude that the test in its present form is of no clinical value.

Kahn and Johnston² have arrived at practically the same conclusions as McLester and Frazier.

GALACTOSE TEST. Pari's³ further experience has confirmed the fluctuations in the response to the galactose test in the same person at different times. Hence, a single test has but little significance. He reports in detail 3 cases of cirrhosis of the liver tested repeatedly for alimentary galactosuria. The response demonstrated that the liver was able to do its work better at some times than at others, its functioning fluctuating with the amounts of ascitic fluid produced, but in the inverse direction.

Test for Urobilin in Urine and Feces. Two reagents are required: (1) a concentrated alcoholic sublimate solution (of about 10 per cent. strength); (2) a 10 per cent. clear, filtered, alcoholic zinc chloride solution and amyl alcohol.

¹ *Journal of American Medical Association*, 1915, lxx, 383.

² *New York Medical Journal*, 1915, cii, 848.

³ *Abstract Journal of American Medical Association*, 1916, lxvi, 90.

Ten cubic centimeters of urine are placed in a test-tube with 5 c.c. of Reagent I, and shaken well with amyl alcohol, using fresh portions of the latter. To the amyl alcohol is added Reagent II. If urobilin is present in pathological amounts, a rose color will appear, even without the addition of the second reagent, but, when the latter is added, a beautiful green fluorescence is seen. The test is not interfered with by anything appearing in normal or pathological urine.

In the feces the test is made as follows: A small portion of the stool is ground with water, Reagent I is added in excess, the mixture again mixed and filtered. To the filtrate, which will be stained pink, Reagent II is added, and green fluorescence is observed.¹

Residual Nitrogen in Liver Disease. Pozzilli² has been applying various tests to 42 persons to ascertain the effect on the composition of the blood of defective functioning on the part of the liver. He studied in particular the functional capacity of the liver for the production of urea, having been impressed by the coincidence of severe liver disease in a number of patients with a pronounced azotemia. He tabulates the findings in regard to the nitrogenous bodies in the serum, the proportion in the form of urea, and the proportion of the non-coagulable nitrogen, the residual nitrogen, classifying separately the 4 normal persons, the 4 with kidney disease but apparently normal liver, the 6 with heart disease plus liver disturbance, 18 with various forms of liver disease, and 10 with respiratory infections, arteriosclerosis or diabetes. The nitrogen coefficient and the automatic regulation of nitrogen balance fluctuate with the intake of nitrogen. The coefficient may further prove misleading in cases of coincident kidney and liver disease, the kidney lesion masking the liver derangement, as the former tends to send up the azotemic coefficient while the liver disease tends to depress it. He emphasizes, therefore, that not the modifications of the azotemic index are significant as to liver disease, but the fluctuations in the residual nitrogen. This is affected but little by the food or by the permeability of the kidney. The proportion of residual nitrogen in the serum depends on the functional capacity of the liver. In health it does not seem to be found in the serum in a proportion higher than 1 per cent. This proportion grows larger when the liver is not working properly, and hence it serves as a simple and reliable index of liver functioning. In short, he declares, azotemia is a well-defined syndrome, and the residual nitrogen in serum bears the same relation to liver functioning that the urea nitrogen in the serum bears to renal functioning. In conclusion he mentions that ligation of the ureters in dogs led to marked increase in the total nitrogen and urea nitrogen content of the serum, but the residual nitrogen was unaffected. On the other hand,

¹ Edelman, *Wien. klin. Woch.*, 1915, xxviii, 978.

² Abstract Journal of American Medical Association, 1916, lxvi, 1065.

ligation of the common bile duct sent up the residual nitrogen content at once.

Urinary Findings in Hepatic Disease. Von Moraczewski and Herzfeld¹ have studied their patients with a view to discovering, if, in hepatic disease, there is a typical urine picture. They examined all hepatic cases, and other cases resembling these, and as further control, healthy individuals. Functional tests were not employed. The authors selected for their studies, ammonia, amino-acids, total nitrogen, uric acid, and purin bases, volatile acids, acetone, indican and indol. The same procedure was followed with diabetes mellitus, pernicious anemia, leukemia and splenic tumor, acid poisoning, and nephritis.

An attempt was made to lower hepatic function by inanition. The periods of feeding were five, arranged as follows:

1. 1 liter milk and 200 grams bread corresponding to 50 grams protein, 40 grams fat, and 150 grams carbohydrates. The caloric content was 1120.

2. 2 liters milk and 400 grams bread.

3. 50 grams cheese, 200 grams bread, 1 liter of tea without sugar, furnishing 620 calories.

4. The same, and 1 kilogram of apple, equal to 1100 calories.

5. 2000 grams potato, equal to 1320 calories.

In the following table, the average of three or four days' observation period is recorded, while in the first column is the count obtained on an absolute starvation day.

	Fasting.	First period.	Second period.	Third period.	Fourth period.	Fifth period.
Urine, c.c.	600	1290	950	1400	1600	1300
Nitrogen, gm.	6.7	13.46	16.05	12.44	9.75	7.17
Uric acid and purin bases, gm.	0.071	0.619	0.407	0.445	0.55	0.409
Ammonia, gm.	0.26	0.432	0.687	0.396	0.623	0.25
Volatile acid	0.297	0.605	0.56	0.45	0.31	0.297
Indican	0.216	0.096	0.04	0.023	0.04	0.061
Acetone, mg.	7.8	0.71	0.77	0.66	0.33	0.61
Indol, mg.	0.93	0.74	0.35	0.33	0.12
Feces, gm.	70	160	100	370	120
Fecal nitrogen, gm.	1.1	1.4	1.4	3.7	1.1
Fecal indol, mg.	10.2	7.2	7.3	8.8	7.6

FIG. 27

In period one, the uric acid, the ammonia, volatile fatty acids, and the indican are relatively high, especially when compared with period two. In this latter, despite twice as much ingested nitrogen, and 3 grams more

¹ Deut. Ztsch. f. klin. Med., 1915, lxxxii, 61.

excreted nitrogen, all other urinary constituents were below those of the first period.

The third period shows the influence of the fat in the diet, otherwise it differs but little from the first period. The uric acid, the ammonia, volatile acids, acetone, indican and indol are considerably less in comparison with the first and second periods. Either this is due to the influence of the fat, or else it is due to the previous rich diet, which may have stimulated the oxidative processes. Previous work undertaken by Moraczewski has shown, however, how unfavorably fat acts on the metabolic processes of the liver, and he believes that it is particularly the milk fat in the third period which has lowered the oxidative power of the liver.

The fourth period was undertaken to demonstrate the influence of vegetable food. By adding apple to the diet, two things are accomplished, first 120 grams of sugar are provided, and second, intestinal resorption is made more difficult. The addition of sugar caused a considerable reduction in acetone and in volatile acids. The uric acid, ammonia and indican remained high. The lowering of nitrogen is but an evidence that carbohydrates spare protein more than does fat. In the first period there was 1120 calories in a diet which contained 40 grams of butter, and the urinary nitrogen was 13 grams; in the fourth period with the same caloric value, but with 120 grams of sugar, the urinary nitrogen was only 9 grams.

The fifth period, on a potato diet, consisting of 2000 grams potato, containing 40 grams protein, 401 grams carbohydrate, or 1320 calories. The urine becomes alkaline on a potato diet which naturally diminishes the amount of ammonia and of volatile acids. On the other hand, it is a purin-poor diet. The excretion of urine indol is interesting, as on this carbohydrate diet the indol was considerably less than in previous periods.

The amount of feces was greatest during the first period (III) also the indol.

Moraczewski and Herzfeld find in liver cases a type similar to hunger cases, *i. e.*, high uric acid, ammonia and acetone values, large amounts of fatty acids and indican. These changes are seen even in mild cases, but when the disease is severe, the changes become more pronounced. In such cases the nitrogen is lowered, and the authors lay much emphasis on "hypazuria." Also weight is laid on the indican output, and it is believed that indicanuria is not alone a sign of intestinal decomposition, but is really dependent to a certain extent on hepatic insufficiency. It is no doubt true that the amount of indican is dependent on indol found in the intestine, but indol can be destroyed or not by the organism, and it is this deficient destroying function which to the writers' minds is a characteristic of hepatic disease. That the urinary indican is not dependent on the amount of indol, is shown in two of their cases:

Case 1. 25 mg. indol in feces = 0.19 indican.

Case 2. 9 mg. indol in feces = 0.39 indican.

The uric acid output is dependent on the amount ingested and degree of combustion. It is impossible to say if a diseased organism can form more purin from a certain amount of protein than a healthy organism, or if it can turn more purin. The authors believe that the increase of urinary acid and purin bases is but a sign that the cells of the body and their nuclein components are being destroyed. Only on this assumption is it possible to compare the increase of uric acid seen both in hunger and in liver disease.

The ammonia increase indicates acid intoxication, and runs parallel with the volatile fatty acids. Acetone is always increased.

These characteristic findings could not be demonstrated in other morbid processes. In other words, in typical hepatic diseases, all urinary constituents selected by Moraczewski and Herzfeld for study were increased, while in other diseases, some were increased and not others, but not all in each case as in liver disease. They do not believe that there is a substance excreted in the urine typical of liver disease, but the important feature is the meeting of many abnormal products. No distinction can be made between icterus catarrhalis and atrophy of the liver. It may be that in icterus, acetone and carbohydrates are more prominent, while in hepatic atrophy the uric acid and the amino-acids (indicating protein destruction).

Obstructive Jaundice. It has long been a well-known clinical fact that, in certain cases of obstructive jaundice, there is a great tendency to hemorrhage. Various causes have been ascribed, delay of fibrin formation (Morawitz and Bierich) decrease in liver function (Kunika), the combination of calcium and bile pigments (King and Stewart), preventing the use of the former for clotting. Lee and Vincent¹ have found no delay in clotting time in simple catarrhal jaundice, but that in obstructive jaundice, with a liver functioning normally, there is a delay. This delay, they believe, is due to a lack of available calcium in the blood and may be more or less counteracted by the administration of calcium lactate by mouth. *In vitro* bile itself prevents coagulation, but it is doubtful if such concentration of bile ever occurs as will prevent entirely the coagulation of blood.

When calcium is given to counteract the tendency to hemorrhage, it must be administered in large doses, and over a period of several days before any marked effect on the coagulation time is observed. If prompt effects, which are, however, transitory in character, are desired, calcium may be given intravenously, apparently without bad results.

Pressure of Bile Secretion during Obstruction of the Ductus Choledochus. Mitchell and Stifel² believe that the pressure in chronic obstruction of the common bile duct rises no higher than in acute obstruction. It may

¹ Archives of Internal Medicine, 1915, xvi, 59.

² Johns Hopkins Hospital Bulletin, 1916, xxvii, 78.

indeed be higher at the end of three hours than at the end of three days. The authors are inclined to believe that it is not on account of the pressure that rupture occurs, but because of the factor of inflammation.

Primary Carcinoma of the Liver. Okazaki¹ examined the accounts of 721 postmortem cases in the pathological laboratory of the Tokio Charity Hospital, and obtained 12 cases of primary cancer of the liver, 1.7 per cent. Splenic enlargement was present in 41.7 per cent., ascites in 91.7 per cent., edema in 66.1 per cent., jaundice in 58.3 per cent. The tumor generally occurred in the right lobe and was either single or multiple. The dissemination through the liver was constant, but in one case the tumor was limited to the right lobe. In 9 cases out of 12 the liver was enlarged. It was normal in 1 case and atrophied in 2 cases. Metastasis was noticed in 7 cases; 7 cases also had a cirrhosis of the liver.

DISEASES OF THE PANCREAS.

Pancreatic Secretion. Schleicher² has made researches on pancreatic secretion in a most painstaking manner, and has examined 22 patients by means of the approved methods. His article contains a brief outline of the individual method employed, and has a full reference appendix which makes the paper particularly valuable. So valuable it is, that I shall quote at length from it, believing that but comparatively few readers of this monograph have had an opportunity of seeing Schleicher's original article. He divides the tests into four groups, those having to do with (I) disturbances of protein digestion, (II) disturbance of carbohydrate digestion, (III) disturbance of nuclear digestion, (IV) disturbance of fat digestion.

I. DISTURBANCE OF PROTEIN DIGESTION. TRYPSIN. 1. *Sahl's Glutoid Capsule.* A formalin-hardened capsule containing iodine, methylene blue and salicylic acid is swallowed, and the urine or saliva is tested at the end of four to six hours. This test has been bitterly assailed, and rightly so, as I have written in preceding numbers of *PROGRESSIVE MEDICINE*, and Schleicher also regards it as unreliable. Schleicher is another observer who finds that gastric digestion plays a greater role than duodenal digestion.

2. *Gelodurat Capsule.* *Schlecht.* The principle of this method is to produce a stool containing large amounts of pancreatic secretion, and to test its powers of digesting a formalinized capsule. Such a capsule containing charcoal is placed in 10 c.c. of the stool (obtained by means of strong purgatives), a few drops of soda solution are added, placed in the oven at 37° C., allowed to digest. Normally, there should be enough

¹ Abstract Journal of American Medical Association, 1916, lxvi, 65.

² Archives f. Verdauungskr., 1915, xxi, 263.

ferment present to digest the capsule in one-half to twenty-four hours. The end-result is seen by the dark appearance of the stool, due to release of charcoal from the capsule. If there is no digestion at the end of twenty-four hours, trypsin is said to be absent. Schleicher has made 93 tests, and thinks the capsules are not specific for pancreatic ferment. Sometimes they are digested by true gastric contents and artificial mixtures within twenty-four hours. Many other objections are brought forward to show according to Schleicher's opinion, the worthlessness of the test.

3. *Plate Method of Müller and Schlecht.* This method requires serum-agar plates, upon which the stool is placed and digestion is allowed to take place. A liquid stool being obtained by purgative, it is mixed with 10 per cent. glycerin water, made alkaline, and small portions are "plated," by means of the platinum loop. The plate is placed in an oven at 50 to 60° C., and if no depressions are seen at the end of twenty-four hours, no trypsin is present. Schleicher has found the method extraordinarily satisfactory and recommends it.

4. *Trypsin Determination. Gross.* The principle of this method is the digestion of casein by trypsin and its precipitation when acetic acid is added. A half-gram of purest casein is dissolved in 1000 c.c. of water containing 1 gram of sodium carbonate. A purgative stool is mixed with three parts of a 1.0% soda solution and filtered. In test-tubes containing 10 c.c. of the casein solution increasing amounts of fecal filtrate are added, and the whole placed in an incubator. Normally, in five to fifteen hours there is no precipitate, showing complete digestion of the casein. Schleicher also agrees that this test is very satisfactory, a conclusion reached by many observers.

II. DISTURBANCE OF CARBOHYDRATE DIGESTION. A purgative stool is filtered, and to increasing amounts of filtrate, 1 per cent. starch solution is added, and the whole incubated for twenty-four hours, at the end of which time the starch digestion is tested by means of $\frac{N}{10}$ iodine solution. Wohlgemuth, who devised the principle of the method, has made quantitative estimations, particularly in urine, Albu has given his approval to the method, and in the praise bestowed upon it, Schleicher concurs with emphasis.

III. DISTURBANCE OF NUCLEAR DIGESTION. SCHMIDT'S NUCLEI TEST. In previous numbers of PROGRESSIVE MEDICINE I have given details of this method, its modifications and the opinion of its supporters and of its detractors, and it will suffice to state that Schleicher is one of the few recent writers who approve of the method.

IV. DISTURBANCE OF FAT DIGESTION. 1. Winternitz. The pancreas is loaded with the digestion of "mono iodinbehensäure ethyl ester," which makes greater demand on the organ than does ordinary fat. If the fat is given on an empty stomach, it is not digested, but should be given with food. Three or four c.c. of the "diagnosticum" are given

with Ewald meal or a cup of milk, and the urine is tested at the end of three to five or ten hours for iodine. A positive reaction indicates good pancreatic functioning. This method meets with the approval of Schleicher.

2. Ehrmann. This test resembles the oil meal of Boldyreff but is much easier to do. Seventy-five grams palmin, a neutral fat containing no fatty acid, are warmed and put in a suspension of 30 grams of rice starch in 250 c.c. of water, a little salt is added, some sodium bicarbonate also, and the mixture is swallowed. After two and a half hours, the stomach is evacuated, the contents shaken with a solution of petroleum ether 90 c.c. and Benzol 10 c.c. (equal parts). The above ether fat layer is put in a test tube and shaken with equal parts of a 3 per cent. cupric acetate solution. If there has been no splitting of fat, the ether layer remains colorless, but if fat has been split, it becomes emerald green. Schleicher believes the Ehrmann test is more satisfactory than the oil breakfast of Boldyreff Vollhard which is to give 200 c.c. of olive oil on an empty stomach and then to remove it at the end of 45 minutes. After centrifugalization there may be seen an oil layer, a bile green layer and a lowermost layer containing ferments. The latter are examined for in the usual manner.

Schleicher regards the Gross test and the Wohlgemuth test most highly, and prefers not to draw any conclusions about the other tests as there have been too few cases.

Diagnostic Value of Amylase in Pancreatic Disease. Using a simplified modification of Wohlgemuth's method, Stocks,¹ finds that any increase of the ferment in the blood serum denotes pancreatic disease, the increase depending on the degree of obstruction in any part of the gland or its ducts, or on the acuteness of the condition. The highest values were found in a case of acute pancreatitis, and Stocks believe that the estimation of the amylolytic capacity of the blood serum and the urine is a most delicate test of the efficiency of the pancreas, and is a most delicate and reliable test for pancreas disease.

Cause of Death in Experimental Pancreatitis. Petersen, Jobling and Eggstein,² injecting bile salts, trypsin and soap as activators, arrive at the conclusion that death, in cases of acute pancreatitis is due to the sudden flooding of the blood stream with the higher split products formed at the expense of the pancreatic tissue, of which the proteose increase is the chief index. Except in the experiments where trypsin was used, there is no increase in serum proteose, which would be the phenomenon if the intoxication were a pure trypsin shock, nor is there much change in serum lipase. There was a distinct increase in anti ferment (protective agent) which apparently favors the recovery of the aminol.

¹ Quarterly Journal of Medicine, 1916, ix, 216.

² Journal of Experimental Medicine, 1916, xxiii, 491.

Pancreatic Calculi. Einhorn¹ gives a review of the literature after 1902, relying on Kinnicutt's paper for articles prior to that time. The condition is a rare one, so that cases are worthy of discussion. Einhorn presents the history of two cases, and regards the following as indicating the correct diagnosis: Colic-like pains, occurring periodically in the epigastrium, associated with a transient glycosuria, are probably caused by a pancreatic stone. The sudden disappearance of the symptoms favors the assumption that the stone has passed. The recurrence of a calculus in the feces, consisting mainly of calcium carbonate and phosphor without cholesterol or bile pigment, points to the pancreatic origin of the stone. At the commencement, and for a long time to come, the process may not at all interfere with the functions of the pancreas. Only later, the presence of a calculus may lead to changes of the pancreatic tissues, which, in turn, causes an impairment of the functions of this organ. The occurrence of sugar in the urine during an attack is of prime importance, although absence of this symptom would not mitigate against the diagnosis of pancreatic stone.

Einhorn recommends medical treatment; rest, warm applications, and opium or atropine, during the attack. Shortly after the attack, frequent small meals and the drinking of alkaline waters are indicated. Should these measures prove inefficacious, an operation should be recommended.

¹ Medical Record, 1915, lxxxviii, 681.

DISEASES OF THE KIDNEYS.

By J. HAROLD AUSTIN, M.D.

BEFORE taking up the diseases of the kidney proper, the writer wishes to devote a few pages to certain studies of the last year upon renal function, diuresis and diuretics, certain histological studies of the changes in the kidney in experimental and spontaneous nephritis in laboratory animals, and certain advances that have been made in our methods for renal functional testing.

Diuresis. Among the experimental studies upon renal function that are of more or less clinical interest, are a number of *researches upon diuresis*. Whether the renal excretory activity is dependent upon nervous regulation, upon the action of a hormone or upon the mere concentration of metabolites, such as urea, or of foreign substances, such as phenolsulphonephthalein in the blood stream, are questions that have a close bearing upon certain of our renal functional tests, upon the validity of certain hypothetical laws of renal activity, such as Ambard's, and upon the theories of the pathogenesis of diabetes insipidus, the action of diuretics, etc. Certain recent experiments which bear upon these questions will be briefly referred to without an attempt to give the details.

Whether there are nerve fibers passing to the kidney, whose function it is to control directly the excretory activity of the kidney, has long been a disputed point. A study by L. Asher¹ suggests that a dual nervous apparatus exists for the kidney, with nerves both for stimulation and for inhibition, but that under ordinary circumstances, the mere presence of metabolites, such as urea, in the circulating blood is sufficient stimulus for the kidney without the intervention of any secretory nerves. R. G. Pearce and E. P. Carter² and W. C. Quimby³ find no evidence in their experiments of the existence of any secretory nerves essential for kidney function.

D. Cow⁴ showed, in 1914, that a physiological amount of normal saline solution may fail to induce diuresis when injected into the circulation, but may give diuresis when introduced by mouth. His further studies suggest that the pituitary gland gives out a diuretic substance to the

¹ Deutsch. med. Wchnschr., 1915, xli, 1000.

² American Journal of Physiology, 1915, xxxviii, 313.

³ Journal of Experimental Medicine, 1916, xxiii, 535.

⁴ Journal of Physiology, 1915, xlix, 441.

blood upon being stimulated by a substance derived from the gastrointestinal mucosa and carried by the blood stream to the pituitary. The exact purpose of this relationship is not at present clear. Its existence has, however, a direct bearing upon the possible relation of pituitary disorder to certain cases of diabetes insipidus.

THE CAUSE OF THE DIURESIS EXCITED BY CAFFEINE has for some time been a subject of dispute. One school has attributed it wholly to the action of caffeine upon the circulation in that it leads to an increase in the rate of blood flow through the kidney, and, as a result of this, to an increased urinary secretion. The other school has insisted upon the importance of a direct stimulating action of the drug upon the renal epithelium. An experiment on the perfused kidney which strongly supports the second view has been carried out by A. N. Richards and O. H. Plant.¹

Caffeine in their experiments caused diuresis in the perfused kidney even when the rate of blood flow through the kidney remained constant. Hence the increase in blood flow which occurs in the intact animal as the result of the action of caffeine upon the renal vessels is not an indispensable factor in the caffeine diuresis.

G. Pierce and A. M. Keith² last year presented work and certain suggestions upon the RELATION OF THE KIDNEYS TO BLOOD-SUGAR AND THE SO-CALLED THRESHOLD PHENOMENON. Most substances in the blood fall into one of two classes with respect to renal function. Either they do not pass through the normal kidney at all, the kidney being impermeable to them, as in the case of the serum proteins, or they are excreted by the kidney whenever present in the blood and the rate of excretion is in some degree dependent upon their concentration in the blood; to the latter class belong urea, uric acid, iodides, most salts, etc. Sugar and certain other substances exhibit a behavior different from either of the groups named. While sugar passes readily through the kidney when present in the blood in excess of a certain concentration, there is an abrupt cessation in its excretion when the blood concentration falls to a certain level. This level is, according to recent work by Keith, about 185 mgm. per 100 c.c. The mechanism by which such a threshold phenomenon can be brought about has been a matter of much speculation. These authors have brought forward certain facts in support of the hypothesis that sugar, when present in the blood below the so-called threshold concentration, fails to appear in the urine because it is oxidized by the renal cells and utilized by them as a source of energy as fast as absorbed. Only when the blood concentration reaches such a level that the absorption of the sugar by the renal cells is more rapid than its oxidation in these cells, does the sugar pass through the renal cells and appear in the urine. In

¹ *Journal of Pharmacology and Experimental Therapeutics*, 1915, vii, 485.

² *Proceedings of Society of Experimental Biology and Medicine*, 1915, xii, 210.

support of their hypothesis is the fact, pointed out by them, that only those sugars which are oxidized in the body exhibit this threshold phenomenon. This same hypothesis might possibly be applied to other substances which find their way through the kidneys only when their concentration in the blood rises above a certain level, if it can be shown that they are substances capable of being metabolized by the renal tissue. Hemoglobin very possibly belongs in this group since, as R. M. Pearce, J. H. Austin and A. B. Eisenbrey¹ showed, hemoglobin appears in the urine only when it has accumulated in the blood above a certain level of concentration, and Hooper and Whipple² have found that other tissues than the liver may produce both bilirubin and urobilin from hemoglobin.

T. Itakura³ has presented evidence of a further relation between the kidney and the blood-sugar. His work, he believes, suggests that there may be some *internal secretion* from the kidney which exerts a regulating influence on the blood-sugar concentration. He found that within an hour to an hour and a half after ligation of either the renal arteries or the renal veins of the rabbit, but especially the veins, there was a pronounced and to some extent, persistent rise of the blood-sugar. Furthermore, he found that this persisting hyperglycemia was markedly reduced, in some cases almost to normal within two or three hours after the injection of about 15 c.c. of blood from the renal vein of another normal rabbit.

Pathological Histology. A number of valuable contributions to the pathological histology of the kidney have been made during the year, and some of these have a definite bearing upon our clinical conception of nephritis. One of the most interesting of these, is the study of W. deB. MacNider⁴ upon the kidneys of dogs exhibiting a naturally acquired chronic nephritis. As the condition is associated with constant or intermittent albuminuria and with the presence of casts in the urine, it is possible to select these animals from a series of dogs and to secure the kidneys at once in various stages of the condition and fixed immediately after death. Opportunity is thus given for a study of the chronic nephritic kidney in certain respects superior to that offered by human material. In all of the 42 cases, there was found a chronic productive nephropathy, in the majority largely confined to the glomeruli and involving both the capillary tufts and the capsules. Indeed, the outstanding characteristic, in this series, was the localization of the kidney injury in the glomeruli. While it may be true that sometimes this was merely an initial step to further damage, it is also true that the essential pathology in these chronic nephropathies may be localized glomerular changes for a long period without the establishment of subsequent

¹ Journal of Experimental Medicine, 1912, xvi, 375.

² Ibid., 1916, xxiii, 137.

³ Mitth. a. d. med. Fakultät der kön., Univ. of Tokyo, 1916, xv, 197.

⁴ Journal of Medical Research, 1916, xxxiv, 177.

changes in other tissues of the kidney. MacNider's findings in this respect are of great interest to the clinician. The identification of the more serious forms of nephritis with the type known as chronic glomerulonephritis has been much emphasized of late. Moreover, Volhard and Fahr laid especial stress upon the early stages of chronic glomerulonephritis, which might be many years in duration, in which they believed the lesions were almost confined to the glomeruli, while the tubules often remained relatively intact. In this stage, the clinical evidences of the disease are albuminuria, casts of various types and elevated blood-pressure, which may be only moderately or extremely high. The renal functional tests in this stage are commonly quite normal, and it is only later, as the tubules become secondarily diseased, that the renal functional tests become impaired and evidences of uremia appear.

It is interesting that many of the kidneys were grossly normal but, in spite of this, exhibited sometimes advanced glomerular disease. That this discrepancy between gross and microscopic findings occurs in the human kidney is known, but cannot be too frequently emphasized. As a rule, the glomeruli exhibited a hyperplasia of fibroblasts as a diffuse process throughout the capillary loops. In a few instances, there was a localization to the base of the tuft. There was usually new connective tissue, obliterating the capillaries, or leaving them with greatly thickened walls.

Some epithelial degeneration and repair was seen in the distal portion of the proximal convoluted tubules and in the ascending Henle loop in some cases.

How readily the changes described by MacNider in the capillaries of the glomeruli could lead to faulty circulation through these vessels can be seen. Whatever the mechanism may be by which the elevation of blood-pressure brought about in glomerulonephritis, the necessity for its existence may readily be surmised.

MacNider¹ has subjected such animals to anesthesia, either with morphine-ether or Gréhant's anesthetic. Following the technic used by him in earlier studies on uranium nephritis, he gauged the functional capacity of the kidney after the development of a state of complete anesthesia, by the rate of urinary flow and by the kidneys' ability to increase the urinary flow in response to certain diuretics: theobromine, urea and glucose. Following the development of a state of complete anesthesia, he found all of the normal animals still diuretic and responsive to diuretic substances. In the nephropathic animals, however, the anesthetic induced a marked effect upon the functional capacity of the kidney, in some experiments the animal becoming acutely anuric following the anesthetic and in other experiments the output of urine being greatly reduced and the kidneys of these animals failing to respond to diuretic substances.

¹ Journal of Medical Research, 1916, xxxiv, 199.

The normal animals showed, on histological examination, normal kidneys except for congestion, shrunken epithelium in the convoluted tubules and fat in the ascending loops of Henle. In the nephropathic animals after anesthetization in addition to the pathology of the chronic glomerulonephropathy there was an acute swelling and necrosis of the epithelium of the convoluted tubules.

Evidently, although the tubules of these kidneys the seat of a chronic glomerulonephritis may appear little, if at all, damaged before the anesthetic, they are, nevertheless, in some way altered so as to be much more susceptible to certain deleterious influences and to readily undergo such degeneration or necrosis as to seriously impair their functional capacity. That the same thing is true in the glomerulonephritis of man, is highly probable.

In chronic parenchymatous nephritis *amyloid* may not infrequently be found in the glomeruli. It is commonly attributed to conditions with long continued chronic suppuration, but C. H. Bailey¹ has demonstrated that it may be produced experimentally in the spleen, kidney and liver, following repeated intravenous injections of living *B. coli communis* even though suppurative lesions did not, as a rule, develop.

An investigation which is interesting in showing what *different types of nephritis may be excited by very closely related toxic substances*, is that of L. Pearce and W. H. Brown² upon the character and distribution of the renal injury produced by various arsenicals. The arsenicals used were arsenious and arsenic acid, salvarsan, sodium cacodylate, neosalvarsan, atoxyl and arsacetin. Some of these produce a predominantly vascular injury, while others produce predominantly a tubular degeneration or necrosis; in addition, the interstitial connective tissue proliferation may be very conspicuous and this may be the case when the vascular injury is only slight.

Renal Functional Tests. A large number of tests for this purpose are now available, many of them of considerable value, and the choice of those best suited for routine use varies somewhat with the individual worker. They may be grouped as follows:

1. Tests based upon the elimination in the urine of dye-stuffs or chemicals (phenolsulphonephthalein, etc.).

2. Tests based on the elimination of water, total nitrogen or urea and chlorides in the urine when, to a standard diet, test quantities of water, urea or salt are added (Albarran, v. Monakow and Pirondini) or when the patient is placed for a test day on a standard mixed diet and the urinary composition is studied at frequent intervals during the day and during the following night. (Hedinger and Schlayer, and Mosenthal.)

3. Tests based upon alteration in the composition of the blood as shown by the freezing point, refractive index, dry residue, protein con-

¹ Journal of Experimental Medicine, 1916, xxiii, 773.

² Ibid., xxii, 442.

tent, total non-protein nitrogen content (or one of its fractions; urea, uric acid, ammonia, amino-nitrogen or creatinin), chloride content or phosphate content.

Of the tests depending upon the elimination of a foreign substance, the phthalein test continues to grow in favor, and supersede the others. A few contributions of special interest have been made during the year to the literature of the test.

THE PHTHALEIN TEST IN ORTHOSTATIC ALBUMINURIA has been studied in seven children by T. C. Hempelmann¹ and the effect of posture on the test determined in these cases. Only marked cases of the so-called lordotic type were used in these studies—cases in which large amounts of albumin appeared in the urine after such a simple procedure as having the child stand against the wall for ten minutes with the heels and back of the head touching the wall, thus throwing the shoulders well back, and bringing the lumbar spine forward. In all cases the urine was free from albumin after a night's rest in bed. It is noteworthy that in all the cases the albumin precipitated on the addition of acetic acid in the cold was very considerable although this precipitate was usually increased by heating. No casts were found in the urine.

Position was without effect upon the phthalein test in normal cases. The phthalein output in the seven abnormal cases in normal position ranged from 58 to 86 per cent. for two hours. When these patients were placed in a lordotic position, producing a marked albuminuria, the total output of phthalein in two hours was reduced on an average 12.9 per cent. The most marked feature, however, was the retardation which took place in the output during the first hour, the average in these cases being 17.6 per cent. less in the lordotic position.

If the above findings may be regarded as lending support to any of the various theories of pathogenesis, it would probably be that one which assumes a mechanical interference with renal circulation as the chief causative factor in the production of an orthostatic albuminuria. Jehle, who has been the most ardent advocate of this theory, believes that the accentuation of the normal forward curve of the lumbar spine so commonly seen in individuals with orthostatic albuminuria, produces an interference with the renal circulation either by compressing or stretching the renal vessels, or otherwise causing a congestion of the kidneys. He does not deny that vasomotor influences may affect the degree of albuminuria, but believes the mechanical factor to be the main feature, without which there is no orthostatic albuminuria. In support of his contention, he submits evidence to show that effacing the lordosis by postural methods causes a disappearance of the albuminuria, and that, furthermore, it is possible to produce an albuminuria in normal individuals by pressure directed through the abdominal wall against the great vessels,

¹ American Journal of Diseases of Children, 1915, x, 408.

or if in animals, by directly constricting or compressing the renal vessels for a short time. Such methods would produce a retardation of the renal circulation, and would probably delay the excretion of a drug, such as phenolsulphonephthalein.

In six cases of orthostatic albuminuria in which the phthalein test was tried by L. F. Barker and F. J. Smith,¹ the excretion was entirely normal in four, and was 5 per cent. lower than normal in one. In the other patient, it was 14 per cent. lower with the patient standing than when made in the recumbent posture. In another case, however, there was no reduction in the amount of dye, even when the conditions producing oliguria and the maximum degree of albuminuria were present.

The kidneys' ability to excrete rapidly large quantities of water ingested, with reduction of the urinary specific gravity, is a simple renal test, which we discussed last year. Albarran administered for such an "experimental polyuria" 350 c.c. of a natural diuretic water, noting the curve of excretion at half hour intervals for the next two hours. Pirondini² has recently devised a somewhat similar test which he calls an "*experimental azoturia*." He gives 10 gms. of urea in 300 c.c. of water and measures the urinary volume and urea output, absolute and relative, at half hourly intervals for three or four hours. He found that the urea excretion, like the water excretion in Albarran's test, reaches its maximum in the third half hour after injection, from which time its excretion curve exhibits a decline which is, however, less steep than the decline of the water curve. The quantity eliminated in the first two hours is approximately 4 grams but this figure varies considerably and may be normally as low as 3 grams. In renal lesions, the urea curve varies from the normal in proportion to the severity in the alteration in renal function, exhibiting disturbances which are readily recognized, such as slowness of urea elimination, dual summits or slow descent of the curve; the elimination of urea in these cases is slow and irregular, there is a diminution in the total elimination and less marked oscillations in the curve. The degree of disturbance is not always, however, proportional to the alteration in the urea excreting coefficient of Ambard.

This method of Pirondini does not appear to the writer to give sufficiently definite results to place it on a par with a number of the other methods of testing renal function. The renal test-meal about to be described seems to him of rather greater value.

A RENAL TEST-MEAL, formulated by v. Monakow, was described in PROGRESSIVE MEDICINE last year, in which the patient was placed on a constant diet, and, when an even output of nitrogen and chlorides had been secured, the ability of the kidneys to excrete promptly an added dose of urea, and, on another day, of sodium chloride was determined.

¹ American Journal of Medical Sciences, 1916, cli, 44.

² Il Policlinico, 1915, xxii, Sez. chir. 259, 294, 326, 398.

The method of v. Monakow has the disadvantage of requiring about a ten day period for completion, accurate collection of all urine during this period being essential. For this reason the method of Hedinger and Schlayer, studying the urinary output and composition during two-hour periods of a single day on a standard renal functional test diet, has obvious advantages. The patient must have been on approximately the same diet for the two preceding days. H. O. Mosenthal¹ and Christian, Frothingham, O'Hare and Woods² have independently simplified the procedure and extended the analysis to include not only water and salt output, as suggested by Hedinger and Schlayer, but also nitrogen, a very important addition to the method. The directions for the renal functional test-meal employed by Mosenthal are as follows:

"All food to be salt-free food from the diet kitchen. Salt for each meal will be furnished in weighed amounts. (One capsule of salt, containing 2.3 gm. of sodium chloride, is furnished for each meal. The salt which is not consumed is returned to the laboratory, where it is weighed, and the actual amount of salt taken is calculated.) All food or liquid not taken must be weighed or measured after meals and charted in the spaces below. Allow no food or fluid of any kind except at meal times. Note any mishaps or irregularities that occur in giving the diet or collecting the specimens.

BREAKFAST, 8 A.M.

Boiled oatmeal, 100 grams.
 Sugar, 1 to 2 teaspoonfuls.
 Milk, 30 c.c.
 Two slices of bread, 30 grams each.
 Butter, 20 grams.
 Coffee, 160 c.c.
 Sugar, 1 teaspoonful. } 200 c.c.
 Milk, 40 c.c.
 Milk, 200 c.c.
 Water, 200 c.c.

DINNER, 12·Noon.

Meat soup, 180 c.c.
 Beefsteak, 100 grams.
 Potato (baked, mashed or boiled), 130 grams.
 Green vegetables, as desired.
 Two slices of bread (30 grams each).
 Butter, 20 grams.
 Tea, 180 c.c.
 Sugar, 1 teaspoonful. } 200 c.c.
 Milk, 20 c.c.
 Water, 250 c.c.
 Pudding (tapioca or rice), 110 grams.

¹ Archives of Internal Medicine, 1915, xvi, 733.

² American Journal of Medical Sciences, 1915, cl, 655.

SUPPER, 5 P.M.

Two eggs cooked in any style.

Two slices bread (30 grams each).

Butter, 20 grams.

Tea, 180 c.c.

Sugar, 1 teaspoonful.

Milk, 20 c.c.

Fruit (stewed or fresh), 1 portion.

Water, 300 c.c.

8 A.M. No food or fluid is to be given during the night or until 8 o'clock the next morning (after voiding), when the regular diet is resumed.

"Patient is to empty bladder at 8 A.M. and at the end of each period, as indicated below. The specimens are to be collected for the following periods in properly labeled bottles, to be furnished by the Chemical Division of the Medical Clinic:

"8 A.M. to 10 A.M.; 10 A.M. to 12 M.; 12 M. to 2 P.M.; 2 P.M. to 4 P.M.; 4 P.M. to 6 P.M.; 6 P.M. to 8 P.M.; 8 P.M. to 8 A.M.

"Specimens are to be left in the ward until called for at 8:30 A.M. by attendant from the chemical laboratory.

"The above dietary contains approximately 13.4 grams of nitrogen, 8.5 grams of salt, 1760 c.c. of fluid, and a considerable quantity of purin material in the meat, soup, tea and coffee. All of these purins act as diuretics, and it is on the mode of excretory response to such stimuli that this method of study of renal function depends." Mosenthal points out that since the food as found in most households suffices to carry out these tests, and the procedure is not a complicated one, it need not be confined to hospitals.

The most important characteristics of the urine in normal individuals on this nephritic test diet are according to Mosenthal:

"1. Variations in the specific gravity of the urine specimens (usually ten points or more).

"2. The balance between the daily output and intake of salt, nitrogen and fluid. This should be approximately equal.

"3. A night urine high in specific gravity (at least 1.016, but usually 1.018 or higher), high in its percentage of nitrogen (above 1 per cent.) and small in amount (400 c.c. or less), regardless of the quantity of fluid ingested or the amount of urine voided during the day."

When kidney function becomes impaired, the changes that occur may be formulated as follows, although this order of events will not follow in every case:

1. Nocturnal polyuria (over 400 c.c.).
2. Tendency to total polyuria (the volume of urine equals or surpasses the quantity of liquids ingested).
3. Fixation of specific gravity, gradually becoming more intense, until it is absolute and the specimens only show a maximum variation of

1 or 2 degrees. In the earlier stages, specific gravity may be fixed at a higher level than later.

4. Fixation of the two-hourly quantities of urine eliminated. That is, the usual polyuric response to meals is absent.

5. The quantity of night urine may diminish to within normal limits. Such night urines, however, are characterized by a low specific gravity and a low percentage of nitrogen.

6. A retention of both salt and nitrogen, which may become very marked.

Such functional pictures, however, are not confined to nephritis. They are found regularly in many other conditions: pyelitis, cystitis, hypertrophied prostate, marked anemia, pyelonephritis, polycystic kidney, and diabetes insipidus. The cause of diminished renal function, it is clear, must be sought for in many directions—the urinary passages, the blood or the kidney itself. Prognosis and therapy will depend largely on the cause of the fundamental impairment and not on its degree. A divergence between the degree of functional renal involvement and the intensity of the signs and symptoms of nephritis is frequently found, and accentuates the lack of parallelism that there may be between functional and anatomical lesion.

“In chronic diffuse (parenchymatous) nephritis, the condition of renal function is characterized by its variability. In these instances, the results of the test-meal have proved to be extremely valuable in giving an idea of the status of salt, nitrogen and water excretion, besides the picture of renal efficiency as a whole. The findings in myocardial insufficiency vary according to the activity of the heart. Distinct differences are found with myocardial decompensation between the period of accumulation of edema, the period of eliminating edema, and subsequently, when cardiac compensation is again fully established. It requires some time before the kidney resumes its normal activity. The intervening period is indicated by a tendency to a low, fixed specific gravity and a nocturnal polyuria. During the period of full myocardial decompensation the results of kidney activity are very characteristic, the specific gravity is markedly fixed at the level of about 1.020, the salt output is diminished, that of nitrogen is high in marked contrast to the salt, and there is oliguria. When chronic nephritis and cardiac decompensation coexist, as they so often do in hypertensive nephritis, the urine may exhibit the characteristics due to either lesion. The determining factor is probably to be found in the chronic nephritis which may or may not be so far advanced as to present an unchanging barrier to the influence of renal congestion.”

The study of renal function by means of the test-meal gives, Mosenthal believes, as valuable information as the longer test of v. Monakow. It is far superior to the experimental azoturia test of Pirondini affording information as to the chloride-handling capacity of the kidney as well as

to its urea-excreting powers, and serving even as regards urea as a much better guide in the regulation of diet. "As a therapeutic guide it is likewise of far more value than any of the tests based upon the injection of dyestuffs or chemicals. It possibly possesses no advantages over the evidence of nitrogen accumulation afforded by direct analysis of the blood or plasma for urea or non-protein nitrogen. These latter methods demand of the patient merely the drawing of the necessary blood from the vein, a procedure often less incommoding, especially to a patient not very ill, than the careful regulation of diet for three days and the accurate collection of urine in periods for twenty-four hours. In a patient very ill, perhaps on the verge of uremia, the test-meal must, of course, be materially modified as such a high salt and protein intake would be injurious." Apparently as regards retention of chlorides, however, the test-meal is proving superior as a guide to dietary regulation, to the estimation of the plasma chlorides. Possibly when we have more studies at hand upon the plasma chlorides, this view may be changed. (For further studies upon the renal test-meal see the quotation from O'Hare, p. 155.)

The Blood in Relation to the Kidneys. ALTERATIONS IN THE COMPOSITION OF THE BLOOD: Butterfield, Erdwurm and Braddock¹ have studied the freezing point of the blood serum as a measure of the concentration of the components of small molecular dimension, such as salts, urea, purins, creatinin, etc., the refractive index, and protein-content as a measure of the solids of larger molecular dimensions, and the dry residue as a measure of total solids. The last three factors may be looked upon from the opposite point of view as rather a measure of the water-content of the serum, diminution in these solids being evidence of hydremia.

It appears from their findings that arteriosclerosis with hypertension leads to the highest concentration of solids in the blood, but that the increase is in the proteins rather than in the salts, urea, etc. In the edema of chronic nephritis precisely the reverse of this picture is found, the solids being low, but again the alteration being in the proteins without much change in the concentration of salts, urea, etc. Cardiac decompensation with edema does not cause any notable change. Chronic nephritis with uremia leads to increase of the salts, urea, etc., as shown by the depression of the freezing point.

As a routine method of study for diagnostic purposes, estimation of the freezing point would seem to have less to commend it than estimation separately of the urea and chlorides of the blood or plasma, unless possibly its simplicity.

NON-PROTEIN NITROGEN OF THE BLOOD. The significance of increased concentration of the non-protein nitrogen of the blood or of its separate components was discussed at length last year. Not much need be added

¹ American Journal of the Medical Sciences, 1916, cli, 63.

to what was said then. One matter of terminology deserves a little emphasis. In some of the discussions of this subject, confusion has been brought about by the use of the term nitrogen-retention or chloride-retention for increased concentration of these substances in the blood. This terminology is natural since the conception usually held is that any considerable increase in these substances in the blood is, in the great majority of instances, due to impaired eliminative function on the part of the kidneys with the resulting accumulation in the blood to an abnormal concentration—a state of affairs to which the term retention might appropriately be applied. The terms nitrogen-and chloride-retention have, however, already been used in a distinctly different sense. By retention in this older sense is meant, of course, an intake of nitrogen or chlorides or other element in excess of its output, as determined in a balance experiment. While nitrogen-retention in this sense might be associated with nitrogen accumulation in the blood, it need not necessarily be so. Nitrogen-retention may occur during growth or the building up of tissue without nitrogen accumulation in the blood. On the other hand, nitrogen accumulation in the blood may persist with a constant non-protein nitrogen concentration of two or three times the normal and yet the daily balance of nitrogen intake and output may be perfect, the impaired kidneys excreting urea at a rate just sufficient to maintain the balance under the whip of the abnormally high urea concentration in the blood. Under these circumstances there is marked nitrogen accumulation in the blood, but, in the proper sense, no nitrogen retention. The writer, himself, has been guilty more than once in the past of having misused the term nitrogen-retention.

V. C. Myers and W. G. Lough¹ have described a method very similar to Folin's for estimating the *creatinin of the blood* which requires about 6 c.c. of oxalated blood. They find that the estimation of the creatinin of the blood is a valuable diagnostic and prognostic test. The creatinin rises above 2.5 mgm. per 100 c.c. (0.9 mgm. of creatinin nitrogen) almost without exception only in conditions with renal involvement. Creatinin values from 2.5 to 3 mgm. (0.9 to 1.1 mgm. creatinin nitrogen) may be viewed with suspicion; figures from 3 to 5 mgm. (1.1 to 1.9 mgm. creatinin nitrogen) are to be regarded as decidedly unfavorable, while over 5 mgm. probably indicate an early fatal termination.

More recently, Myers, Fine and Lough² have studied the uric acid, urea and creatinin in a series of chronic nephritics. The permeability of the kidney is impaired in these cases, as indicated by an increase first of uric acid, later of urea, and lastly, of creatinin. These findings are not entirely in accord with those of Woods to be detailed.

A. C. Woods³ has studied the *nitrogen partition in the blood and spinal*

¹ Archives of Internal Medicine, 1915, xvi, 536.

² Ibid., 1916, xvii, 570.

³ Ibid., 1915, xvi, 577.

fluid of 18 cases with special reference to the possible causation of albuminuric retinitis.

Chauffard attempted to explain albuminuric retinitis on the grounds of a hypercholesterinemia, while Onfrey and Balavoine attempted to show that changes in the viscosity of the blood played an important part. The theory that attracted the greatest amount of attention, however, was that advanced by Widal, in 1910. He stated that albuminuric retinitis was the result of the retention in the blood of urea or of some nitrogenous body closely allied to urea.

In Woods study estimations were made of the total non-protein nitrogen, of the ammonia nitrogen, of the urea nitrogen, the uric acid, creatinin, combined creatinin and creatin and of the amino-acid nitrogen of the blood. Estimations were also made of the total non-protein nitrogen and urea nitrogen in the spinal fluid taken at the same time as the blood.

While the highest accumulation observed, 266 and 257 mg. of non-protein nitrogen per 100 c.c. of blood, happened to occur in cases of albuminuric retinitis, nevertheless marked retinitis occurred at practically any level of nitrogen accumulation. There appears to be no close relationship whatsoever between either total non-protein nitrogen accumulation, or any component part, and the occurrence of albuminuric retinitis.

The uric acid figures were the last to show any marked increase as the total non-protein nitrogen rose. Only 2 cases showed any marked uric acid retention. In these 2 cases blood was taken thirty-six and twelve hours before death. The creatinin showed roughly a proportionate increase as the total non-protein nitrogen rose, averaging in all 3.4 per cent. of the total non-protein nitrogen.

"In the limited number of cases in which as complete partitions as possible were done, figures are given showing the 'residual nitrogen.' These figures were obtained by subtracting the sum total of the determined component nitrogen constituents from the total non-protein nitrogen. These figures are of interest in that they seem in several cases to run roughly parallel with the severity of the case as observed clinically." "The urea content of the spinal fluid throughout approximately equaled that of the blood, as shown before by Widal, Javal, and others. It does not seem probable that nitrogen determinations in the spinal fluid give any greater diagnostic or prognostic significance than those in the blood."

Woods findings regarding the late rise of uric acid in the blood are not, it will be seen, in harmony with those of Myers, Fine and Lough just quoted.

Tileston, Wilder and Comfort¹ made a study of the *total non-protein*

¹ American Journal of Diseases of Children, 1915, x, 278.

nitrogen and the urea of the blood by the method of Folin and Denis in a series of children and also carried out the phthalein test by the usual technic obtaining the urine in every instance by catheter.

Blood in the case of children over two years of age was taken for examination before breakfast after a twelve hours' fast, as considerably higher figures were sometimes found at other times of the day. However, in the case of children acutely sick and taking in consequence less than the accustomed amount of food, the blood may be taken at any time of the day without the liability of error.

The Phthalein Excretion in Normal Children was found to vary from 35 to 64 per cent. for the first hour, and from 17 to 44 per cent. for the second hour. The total excretion for the two hours was much more constant, from 78 to 81 per cent.

From this study one may conclude that in the acute infections of children, the phthalein test may show pronounced depression without apparent cause, and but little significance should be attached to such a finding unless there are associated signs of nephritis. An increase in either blood urea or total non-protein blood-nitrogen in these cases is the rule in cases tending toward uremia, and these tests should be of diagnostic value.

The blood, however, must be taken before the morning feeding, after several hours' fasting, otherwise a misleading elevation of the figures may result from the influence of the food.

H. T. Karsner, H. A. Bunker and G. P. Grabfield¹ studied in dogs the influence of reduction of the kidney substance by partial excision upon the non-protein nitrogen of the blood and upon the urinary output and excretion of urea. The animals were kept on a diet of dog biscuit. Passing over the influence of the operation *per se* during the first twenty-four or forty-eight hours, it was found that removal of one-sixth or one-half of the kidney substance led to no increase in the non-protein nitrogen of the blood. Removal of approximately two-thirds of the kidney substance led to a slight increase persisting several days. The urine at the same time was normal in amount and concentration. Diarrhea occurred frequently even after excision of only one-half of the kidney substance. Following complete removal of the kidney substance, a rapid rise of the non-protein nitrogen in the blood occurred, the increase being about 60 mgms. per 100 c.c. of blood per day. Death occurred on the third or fourth day.

During the past year, Bang² has published a small monograph detailing his methods for *microchemical examination of the blood* for the following components: chlorides, non-protein nitrogen, urea, coagulable protein, blood sugar, fat, total dried substance. For each of these exami-

¹ Journal of Experimental Medicine, 1915, xxii, 544.

² Ivar Bang, Methoden zur Mikrobestimmung einiger Blutbestandteile, Wiesbaden, 1916.

nations he uses two drops of blood from the finger or ear received on a small piece of specially prepared absorptive paper.

Bang presents detailed studies to establish the accuracy of these methods and considers that they compare favorably with the other methods available for the same components.

At first sight, that in these methods only two or three drops of blood from the finger is required and that it is unnecessary to enter a vein, might appear to offer considerable advantages over such methods as Folin's, Van Slyke and Cullen's urease, Bloor's methods for blood fats, etc. The writer does not believe, however, that for ordinary routine work this is the case. When working with such minute quantities of blood, the extraordinary precautions which one must take to secure sufficiently pure reagents and to keep these and the apparatus uncontaminated in the minutest degree, renders the laboratory work distinctly more arduous and much more subject to unforeseen errors than is the case with those methods just mentioned and similar ones devised in the laboratories of this country during the last few years which employ from 1 to 10 c.c. of blood for analysis.

Possibly Bang's methods might be desirable for certain studies where it is necessary to analyze the blood at frequent intervals, but because of their admittedly greater error, they cannot be used to detect such small changes as can other methods and their value for this purpose is consequently limited. Using these methods, Bang has published the results of studies of the total nitrogen and urea in normal individuals, certain species of animals, and in experimental conditions, such as fasting, after feeding, in nephritis from various toxic agents and in phosphorus poisoning. He has divided his total non-protein nitrogen into two fractions—the urea fraction, including ammonia, and the remainder to which, unjustifiably, he gives the name amino-acid fraction. Bang, himself, recognizes that this fraction includes not only amino-acids, but also uric acid, creatinin and other components, but he assumes that the amino-acids constitute so much the larger part of the group as to warrant so designating the whole fraction. Analyses of the amino-nitrogen of the blood by the Van Slyke method do not support this view, even in normal blood. In nephritic blood, moreover, the uric acid and creatinin values may far exceed the amino-nitrogen of the blood, rendering Bang's assumption in nephritic studies highly misleading.

A valuable study of the effects of *phosphorus poisoning* and also of *chloroform poisoning* is that of E. K. Marshall, Jr., and L. G. Rowntree.¹ They find that the total non-protein nitrogen, urea and amino-acids of the blood serum show a definite and sometimes marked increase in phosphorus poisoning. These changes are not so evident in chloroform poisoning, although they sometimes occur. They are usually terminal

¹ Journal of Experimental Medicine, 1915, xxii, 333.

phenomena. This increase of the nitrogenous products in the blood is associated with an increase of these substances in the urine except that there is a very low urea N percentage in the urine in severe, fatal chloroform poisoning. Hence the increase in the blood cannot be attributed wholly to a renal insufficiency, but must indicate an increased protein katabolism, as well as renal insufficiency, to explain this accumulation. Terminal acidosis, as evidenced by increased hydrogen-ion concentration in the blood, usually occurs.

H. Davis and N. B. Foster¹ have shown that the accumulation of urea and other forms of non-protein nitrogen is not only in the blood in nephritis, but in the tissues as well.

A study of the *blood-urea findings before and after anesthesia* by D. F. Cameron² is of much interest.

The effect of nitrous oxide-oxygen-ether anesthesia with rebreathing, very little ether being used, was studied on 13 patients. The blood-urea determinations were made twenty-four hours or less before operation, and from twenty-four to forty-eight hours afterward, and sometimes subsequently, at from three- to five-day intervals. All patients except one showed a more or less marked rise in blood-urea immediately following operation, the average being 21 mgm. per 100 c.c. of blood. Another study was made of the blood-urea findings before and after ether-anesthesia by the open method in twenty-five miscellaneous cases:

Apparently the increase in blood-urea concentration following operation under gas-oxygen-ether anesthesia was slightly greater than the increase following similar operations under ether.

Ambard and Weill's Coefficient of Urea Excretion. Reference was made last year to Ambard and Weills' coefficient and to a simplification of it by McLean. A more recent description of his method and a discussion of its value has been published by McLean.³ He shows that a nephritic with distinct impairment of the urea-excreting function of the kidney may show increase of the blood-urea upon an ordinary diet, or a marked increase of blood-urea upon a very high protein diet; but blood-urea figures within the range ordinarily accepted as normal if on an extremely restricted protein diet. Yet such a patient, even in the third instance mentioned, will show the same lowered index of urea excretion that he shows when on a high diet. Thus the renal impairment can be recognized by the index while it might be overlooked by the simple estimation of blood-urea. A very close parallelism was observed between the phthalein test and the urea index. "An index below 80 is to be considered as abnormal, though not necessarily seriously so. In renal disease, an index below 50 is indicative of a considerable degree of impairment of functional ability. The amount of damage to the kidneys, it is

¹ Proceedings of the Society of Experimental Biology and Medicine, 1915, xiii, 33.

² Journal of the American Medical Association, 1916, lxvi, 1765.

³ Ibid., 1916, lxvi, 415.

believed, is increasingly greater as the index is lower, and tends to approach zero. But a low index may be only temporary, as in the passive congestion of heart failure or in acute nephritis, and may return to normal on improvement in the condition which is responsible for impaired function. A low index has at times been the first indication of a serious kidney involvement. When the condition is stationary, life can be maintained for some time with a low index, for example for several months with an index of from 5 to 8;" and he has seen recovery from an acute nephritis in which the same figures were obtained. One patient survived a month with an index of 1.2.

Regarding the use of the index as a guide to treatment, McLean questions whether the reduction in the blood-urea that follows a very low nitrogen intake has any direct beneficial effect. "On general principles, an impaired function should not be overtaxed, and a restricted protein intake should be advised in cases with a markedly lowered index of excretion. But brutal restriction of nitrogen intake to below the requirement of the body does not seem to be indicated in cases capable of excreting normal amounts of urea, though the blood-nitrogen may be high and the index low." For diet regulation, therefore, McLean would apparently be guided rather by the kidneys' ability to maintain a balance of nitrogen output and intake upon a given diet than by the degree of nitrogen accumulation in the blood or the lowering of the index. Whether brief rest periods on a protein starvation diet, for a few days only at a time, would improve the renal condition, only carefully controlled studies will show.

Certain objections may very properly be raised to accepting the Ambard-Weill coefficient or its modification, the index of McLean, as an altogether satisfactory criterion of renal efficiency.

T. Addis and C. K. Watanabe,¹ in the course of an investigation into the factors regulating the rate of urea excretion, have accumulated figures which bear directly on the question of the validity of Ambard and Weill's laws and the formula based on these. These laws are:

1. If the concentration of urea in the urine is kept constant, the square root of the amount of urea eliminated in a unit of time is closely proportional to the concentration of urea in the blood.

2. If the concentration of the blood-urea remains constant, the amount of urea excreted in a unit of time is inversely proportional to the square root of the concentration of urea in the urine, or graphically:

$$\frac{D_1}{D_2} = \frac{\sqrt{C_2}}{\sqrt{C_1}}$$

D being the amount of urea excreted and *C* being the concentration of urea in the urine.

¹ Journal of Biological Chemistry, 1916, xxiv, 203.

As may be seen by reference to the original studies of Ambard, these laws are not based on very many individual experiments, and it must be remembered that they are wholly empirical laws, not founded upon any fundamental physical basis. Especially Ambard's second law rests upon very scanty experimental proof, being deduced from a single experiment on each of two individuals.

Addis and Watanabe grouped the analyses which they had at hand upon a series of cases, some with normal and some with increased blood-urea, so that those exhibiting the same urea concentration in the urine might be used to test the validity of Ambard's first law and those exhibiting the same urea concentration in the blood, to test Ambard's second law. They were quite unable to confirm either of the laws by this method. Variations from the theoretical values of over 100 per cent. were common. They say: "We believe it is important to demonstrate that the factors governing the excretion of urea by the kidneys are not fully known, for the impression that they are not only known, but are measurable with mathematical accuracy is likely to retard further investigation. The approximate constancy of the combined formula, which after all, is only roughly approximate, is due in part to the tendency for increased urea concentration in the blood to be accompanied by an increased rate of urea excretion. But in larger part, it is to be ascribed to its mathematical construction. The more variable factors—the concentration in the urine, the volume of urine, and the amount of urea in the urine—occur as the square or fourth roots of their values. Their disturbing effect on the constancy of the resultant formula is thus greatly reduced, while the only factor used without such modification—the concentration of urea in the blood—is itself the most constant quantity used."

Very similar conclusions were reached by L. Jonas and J. H. Austin.¹ A study of the urea index of McLean, determined upon a number of individuals with presumably normal kidneys, yielded very variable figures. Attempts to verify the two laws separately met with moderate success as regards the first law, but none as regards the second. This finding is in harmony with the results obtained by Pepper and Austin² in a study of the blood and urinary nitrogen of dogs under varying conditions. Jonas and Austin conclude that Ambard's formula or its modification in the McLean index is not a mathematically accurate expression of the behavior of renal function as regards urea, but merely an approximate indication of certain relations between blood-urea and urea excretion and urinary urea concentration. The determination of the index, because of the necessity for great accuracy in collection of the urine is a much more difficult procedure to carry out than is the

¹ American Journal of the Medical Sciences, 1916, clii, 560.

² Journal of Biological Chemistry, 1915, xxii, 81.

simple estimation of the blood-urea, and more important still there are possibilities of undetected errors occurring through the loss of a small quantity of urine. Hence, unless some definite advantage can be urged in favor of the quotient as compared with the simple blood-urea considered with due regard to the character of the urinary excretion, the latter would appear to be the safer criterion in clinical diagnosis and prognosis.

Accepting 0.35 gm. of urea per liter of blood as the upper limit of the normal on an ordinary protein intake, the index proved no more delicate or accurate guide in the recognition of renal impairment in their series of nephritic cases than did the blood-urea alone. In cases in which in all probability the only impairment in renal function is the result of arteriosclerotic changes or renal passive congestion, the index may show pronounced depression while the blood-urea remains within normal limits. There is evidence to suggest, therefore, that the index is, at least in certain cases, a more delicate gauge of renal impairment than is the blood-urea. It is at least possible, however, and indeed highly probable, that for clinical purposes of diagnosis and prognosis these cases present rather an argument against the use of the index and for the blood-urea than the reverse. It is in part because the estimation of the blood-urea often helps to distinguish true nephritis from arteriosclerotic lesions, or from congestion of the kidneys, that it is of value in these cases. Clearly, for this purpose, the index would be of less value, being too sensitive and too readily reduced by arteriosclerotic conditions and by passive congestion as well as by nephritis. It seems possible that in conditions in which there is either an extremely high nitrogenous intake or in which there is very rapid tissue catabolism, the blood-urea may be raised above 0.35 gm. per liter, although renal function is quite normal, and that this may be accompanied by an increased rate of urea elimination in the urine with a normal index. In such cases the index would be a better gauge of the state of renal efficiency than would be the blood-urea alone. McLean has induced just such a condition by the administration of urea to normal individuals. Under ordinary circumstances, however, such conditions do not obtain, and our conclusion would be that, as a rule, the blood-urea alone is a better guide in ordinary clinical diagnosis and prognosis than is the index.

J. P. O'Hare¹ has compared the excretion of urea and salt added to a standard diet (v. Monakow's test), the two-hourly excretion upon the one day test diet of Hedinger and Schlayer (see p. 144), the phthalein excretion, blood-nitrogen or blood-urea and in a few instances the McLean index for urea and chlorides in a series of 30 cases of nephritis of various types and grades of severity, and in 4 cases without renal lesions.

¹ Archives of Internal Medicine, 1916, xvii, 711.

Using the test diet the chloride excretion was found as a rule to be more seriously, and presumably more quickly, affected than the nitrogen excretion.

The test diet is by no means without faults, he concludes. The most important is that it cannot be used in all cases of chronic nephritis. In very severe cases, of course, no such diet can be taken, even when the heavy noon meal is modified, as was done for some patients. This modification, of course, may interfere more or less with the results, inasmuch as the reduction in the meal may just fail to show fixation when the full meal would do so.

"In some cases the patient is made temporarily worse by the full test diet. Then, too, digestive disturbances, indicated by distress after the noon meal, may cause a delayed absorption in the stomach and intestines. The various elements then get to the kidneys slowly and in small amounts. This would, of course, interfere with the proper interpretation of results. Cases with edema cannot be studied very satisfactorily because of the unstable water metabolism."

A very close parallelism was observed between the Monakow test and the two-hourly excretion on the test diet.

"It would seem indeed that the indices of urea and salt excretion, especially the former, as determined by Ambard's or McLean's formulas, are more satisfactory tests of renal function than are the test diets, as they give us as much information as any of the other tests, especially in the milder cases; they are distinctly shorter than the dietary tests since they can be completed in two hours, if necessary, and they are not especially difficult to carry out. The phenolsulphonephthalein excretion, to be sure, is less difficult of determination than any of these, but it is by no means satisfactory in cases of chronic nephritis because in the earlier stages of the condition it may be essentially normal, although there are definite disturbances in salt, nitrogen or water excretion. A simple determination of blood-nitrogen similarly may give normal figures in milder cases, while the calculated index of excretion is distinctly abnormal. For the determination of these indices of excretion, no dieting or preliminary preparation is required and the determination can be made on all but moribund patients. Hence they have an advantage over the longer dietary tests."

As already indicated, the writer is disposed to draw his conclusions concerning the nitrogen eliminating function directly from the blood-urea or total non-protein nitrogen of the blood, paying due regard to the character of the patient's diet and perhaps to the daily nitrogen excretion absolute and relative, rather than from the quotient of Ambard or its modification by McLean. With regard to the question of chlorides, he will present his views after discussing another important paper.

CHLORIDE EXCRETORY FUNCTION. The most valuable study of the year with regard to the chloride excretory function is probably that of

C. C. Wolferth.¹ His study is designed to determine the value as a clinical test of the method of measuring the sodium chloride excretory function recently introduced by McLean and briefly referred to in *PROGRESSIVE MEDICINE* last year. This method consists of estimating the plasma chlorides, the output of chlorides in the urine and their concentration, and using these factors in a slight modification of Ambard's formula for chloride excretion. The method is analogous to the Ambard quotient or McLean index for urea. The formula is based on the view that the rate of sodium chloride excretion is dependent upon the excess of sodium chloride in the plasma above a certain threshold, and upon the rate of water excretion, and that this threshold is fairly constant in the normal individual at about 5.62 gm. per liter of plasma, so that its rise is an indication of an impaired elimination of chlorides.

Wolferth's study comprises 78 determinations of the plasma chlorides and of the calculated chloride threshold in 47 individuals. Of these, 10 were without renal disturbance, cardiac decompensation or edema, and showed normal figures for plasma chlorides and threshold. In these cases the threshold showed a variation of only from +0.12 gm. to -0.18 gm. from the standard threshold, a variation a trifle less than that observed by McLean in his normal cases. Seven cases were presumably non-nephritic, but showed elevation of the plasma chlorides and of the threshold. In 5 of these, this elevation was presumably due to circulatory disturbances with edema. One was an habitual user of large amounts of salt with an edema that disappeared when he was placed on a salt-free diet. In the other case, the chloride disturbance was unexplained.

Among the nephritic cases, of 11 diagnosed clinically as advanced glomerulonephritis, 9 showed a high chloride threshold. One of these, after a prolonged period of salt-free diet, exhibited an actual plasma chloride concentration below the normal threshold, but two days after the administration of 10 gm. of sodium chloride, the plasma chlorides and the threshold had again risen slightly beyond their original point. Of the 2 cases of glomerulonephritis that never showed elevation of the chloride threshold, although there was in both marked elevation of the blood-urea and marked reduction of the phthalein, in 1 case to a trace, 1 case, at least, had been on a salt-free diet for some time before the determination of the plasma chlorides.

It is noted, however, that 3 cases in this nephritic group showed no reduction of their elevated chloride threshold in spite of a course of vapor baths and salt-free diet. Apparently, the level of the threshold for chlorides is, in some cases, greatly reduced by prolonged salt-free diet just as conversely, among the non-nephritic cases, 1 was observed

¹ American Journal of the Medical Sciences, in press.

with a very high threshold for chlorides following long continued excessive ingestion of chlorides. Two cases, one already mentioned, are of especial interest, in that they show that even when the plasma chlorides and chloride threshold are very low following a prolonged salt-free diet, the ability to eliminate chlorides may still be impaired, as indicated by the fact that added chlorides are poorly excreted and force the plasma chlorides and threshold to a high figure.

Two out of 4 cases of less advanced glomerulonephritis showed elevation of the plasma chlorides and chloride threshold. One of these was interesting in that in spite of a high chloride threshold his ability to excrete added salt was practically unimpaired.

In two cases of chronic parenchymatous or degenerative nephritis, the elevation of the chloride threshold was more pronounced than the disturbance of phthalein or urea excretion. The two cases of renal sclerosis studied showed no disturbance of the chloride threshold. A case of acute pyelonephritis, confirmed by autopsy, with a blood-urea of 442 mg. per 100 c.c. and a phthalein excretion varying from 10 per cent. to a trace, showed a low chloride threshold; the character of this patient's diet is not stated. Two cases of mercuric chloride poisoning are interesting in that, during the period of very intense diuresis induced by the Lambert treatment, their plasma chlorides and chloride threshold were considerably below the normal, while after cessation of this diuretic treatment, they rose to somewhat above normal. The 5 cases of eclampsia all showed a high plasma chloride concentration, and the 3 in whom urinary studies could be carried out showed marked elevation of chloride threshold. The two pre-eclamptics also showed chloride accumulation. Wolferth notes that this chloride accumulation is in contrast to the very slight tendency for the non-protein nitrogenous substances to be increased in eclampsia. Wolferth's conclusions are as follows:

"1. An elevated plasma chloride threshold, when circulatory disturbances can be excluded, is valuable evidence of the presence of nephritis.

"2. A normal threshold may be found in cases with marked impairment of ability to excrete chlorides, particularly if the patient has been kept on a régime including salt-free diet and measures to stimulate elimination.

"3. Sodium chloride added to the diet is sometimes excreted as completely by impaired kidneys working under the stimulation of a high chloride content of the plasma as by normal kidneys working under normal threshold; added chloride may be retained when the threshold is normal. Therefore, the information gained by both methods of study is desirable.

"4. Chloride excretory function is impaired in nearly all cases of nephritis.

"5. Chloride excretory function is much more disturbed in eclampsia, than is urea excretory function."

From an analysis of Wolferth's findings, as well as of the other investigations thus far published on this subject, the writer is inclined to question the validity of Ambard's conception of a chloride threshold. Clearly it would seem that no such constant threshold as Ambard supposes exists. By withholding salt over some period of time, or by very free administration of water with excessive diuresis even for a short period, one can frequently reduce the plasma chlorides far below Ambard's threshold. Conversely, excessive ingestion of salt will raise not only the plasma chlorides but the threshold calculated by Ambard's formula.

We do not yet possess, the writer believes, the formula that expresses the normal relation between the plasma chlorides and the urinary excretion, and probably in dealing with chlorides such a formula is not possible unless in it be included a factor that takes account of the rate of chloride intake. Whether or not still other extra-renal factors must be taken into account, as it is well known they must be in considering the relation of chloride intake to chloride output, also awaits investigation.

It is certainly quite clear, both from O'Hare's and from Wolferth's study, that the concentration of chlorides in the plasma bears no constant relation to the capacity of the kidneys to excrete chloride added to the diet. Which is the better gauge of renal function only further investigation can tell. Almost certainly both are to a large extent influenced by extra-renal factors.

For the present, therefore, the author believes it is premature to use either the chloride excretion, the concentration of plasma chlorides or the chloride threshold calculated by Ambard's or McLean's formula for the diagnosis of renal excretory function with respect to chlorides. This whole subject belongs still in the field of clinical and experimental research, but in this aspect presents itself in a highly promising light.

Further studies have been made during the past year upon the *acidosis occurring in renal disease*. A few words may be said about the acid-base equilibrium in the blood. Owing to its peculiar composition, the blood possesses remarkable powers of absorbing acids or alkalis with little change in its own reaction. This capacity is most essential to the organism for it makes possible the transfer of acids or alkalis from the point of origin or absorption to the eliminating organs without significant change in the reaction of the transporting fluids, a change which did it occur in more than a very small degree would destroy the life of the cells in contact with the fluid. This constancy of reaction in the blood, so essential to life, is secured largely by the presence of the sodium salts of certain weak acids, chiefly carbonic and phosphoric acids. It is these salts, and especially the carbonates, which are in the

main responsible for giving the blood its capacity for taking up acids or alkalies without a change in its own reaction. When the blood takes up acids, the sodium of the carbonates effects a neutralization of the acid and the carbon dioxide set free is removed through the lungs, while the carbonates of the blood are decreased. Similarly, the base of the phosphates neutralize acids introduced, and the acid phosphate left is eliminated through the kidneys.

To these substances, the carbonates and phosphates of the blood, because of their behavior with relation to acids and alkalies, Henderson has given the name of "buffer substances." Acidosis may be defined as an abnormal diminution in the amount of these "buffer substances" in the blood (Henderson). A number of secondary effects are consequent upon this reduction, tending to restore the normal condition. The most constant of these is stimulation of the respiratory centre with increased ventilation of the lungs. This in mild acidosis can be detected only by measurement of the carbon dioxide content of the alveolar air which will be found below normal; in severe acidosis the deepened respiration at an increased rate constitutes the most characteristic feature of the clinical symptom-complex. The kidneys, if their activity is not impaired, excrete an increased quantity of acids, and the urine can be rendered alkaline only by the administration of a larger dose of soda or other alkali than is required in the normal individual. The ammonia of the urine may be abnormally high due to the formation of this substance from protein in the body in order to serve in the body as a base and spare its fixed bases. In the acidosis of renal disease, however, the ammonia excretion is usually lower than normal, as shown by Henderson and Palmer, as the kidney's capacity for excreting this substance seems to be impaired. In its mildest forms, acidosis can be detected only by use of some special test, one of the laboratory methods. The term, acid intoxication, however, may be used for the severer grades of acidosis with a clinical symptom-complex of which the most characteristic feature is the peculiar hyperpnea without cyanosis.

The acid bodies responsible for acidosis are not the same in all cases. In starvation, on a protein-fat diet, in diabetes mellitus, and in surgical anesthesia, they are chiefly the ketone bodies. The same probably is true of most of the severe acid intoxications of childhood. On the other hand, in nephritis and in the severe diarrheas of children, Howland and Marriott¹ have found evidence that retention of acid phosphates is largely responsible for the condition.

For the recognition of acidosis, we have available a number of methods. The condition may be suspected on the basis of the symptom-complex of acid intoxication. To rest the diagnosis on this basis alone, however, will lead to a certain percentage of error, for further investigation by

¹ American Journal of Diseases of Children, 1916, xi, 309.

special methods has repeatedly failed to reveal acidosis in a proportion of cases at first so diagnosed on symptoms alone.

Again there are many mild forms of acidosis, and some of moderate grade, which are not severe enough to give the clinical picture of acid intoxication, and which, arising from other acids than the ketone acids, cause no acetone or diacetic acid to appear in the urine. This especially holds for the acidosis of renal disease. For the recognition of these and for the more accurate diagnosis of all forms of acidosis, it is very desirable to use one of the newer methods now available. These include the Van Slyke-Stillman-Cullen method¹ for determining the carbonate content of the blood or Marriott's² method for determining the hydrogen-ion concentration of the serum. About 5 c.c. of blood is employed in either of these methods, although they can be carried out with somewhat less, and the technic requires about the same degree of familiarity with laboratory methods as does the determination of blood-urea.

Next to these in value is the estimation of the carbon dioxide content of the alveolar air. A very simple method for this has been devised by Marriott and recently published,³ and Howland and Marriott have adapted it for use with infants and young children. It can be carried out in a few minutes in the office as well as in the hospital ward, but there is undoubtedly opportunity for errors from faulty methods of breathing on the part of the patient, and, moreover, the placing of the air tight mask over the patient's mouth, especially in a nervous or dyspneic patient has, in my experience, caused much more dismay and anxiety on the part of some patients than the removal of a little blood from a vein.

One of these methods ought, I think, to be added to the equipment of every good hospital laboratory for routine use in the study of all patients in whom acidosis might be suspected, or indeed, until our knowledge of this subject is greater, upon all patients.

J. H. Austin and L. Jonas⁴ have applied some of these methods, and especially the Van Slyke-Stillman-Cullen method, to a series of clinical cases. They found that by the Van Slyke method the CO_2 capacity of the plasma is slightly reduced in arteriosclerotic conditions and moderately to markedly reduced in diabetes and nephritis, especially in the advanced stages.

After ether anesthesia there is a moderate depression of the CO_2 capacity of the plasma. This depression is proportional to the duration of the anesthesia, is present and probably maximal at the close of the anesthesia, and apparently remains little altered for at least five hours.

It is interesting that two cases of acute bichloride poisoning which at

¹ Proceedings of the Society of Experimental Biology and Medicine, 1915, xiii, 165.

² Archives of Internal Medicine, 1916, xvii, 840.

³ Journal of the American Medical Association, 1916, lxvi, 1594.

⁴ American Journal of the Medical Sciences, in press.

first had reduction of their phthalein output but no increase of blood-urea exhibited normal blood CO_2 figures, 70 to 71 volumes per cent. Both cases were on the highly diuretic and alkaline treatment of Lambert, however. Five eclamptics all showed an acidosis, the figures ranging from 46 to 57 volumes per cent.

Another test of acidosis is Sellard's,¹ the determination of the amount of soda that must be given a patient to render the urine alkaline to litmus. Four grams suffices in the normal individual. Two, three or four times this amount, or sometimes much more, depending upon the grade of the acidosis, will be required in cases of acidosis. If there be no cystitis to alter the reaction of the urine between the kidney and the test-tube, this simple test is of considerable value.

For the treatment of the mild or moderate acidosis of renal and cardiorenal disease, promotion of diuresis is the rational procedure. Alkalies act in these cases not only by adding base to the blood, but by promoting the excretion of acids through the kidneys. Alkali may be given as an alkaline diuretic avoiding, however, large doses of potassium salts (see p. 159) or more simply in the form of sodium bicarbonate in a 2 to 5 per cent. solution by mouth.

The dosage is best regulated by observing the effect on the reaction of the urine. This should be rendered less acid, but not distinctly alkaline. If the urine be diluted with 15 parts of water and a drop of alizarin sulphonate added, it will react before treatment distinctly acid; when sufficient soda has been given, the diluted urine will be red to alizarin but should still be colorless to phenolphthalein. If there be no cystitis to alter the urinary reaction, this serves as the best guide to dosage. Normal urine is rendered distinctly alkaline by 4 grams of soda. While in the milder forms of acidosis alkaline therapy is not necessary, it is probably never detrimental if not carried to the point of rendering the urine strongly and persistently alkaline.

The writer presented last year some of the conflicting views upon *the portion of the uriniferous tubule from which various substances are excreted*. He showed that there was strong evidence against the view of Schlayer, von Monakow and Volhard and Fahr that urea is excreted chiefly by the glomeruli, chlorides chiefly by the tubules. The various substances excreted do not appear to fall into two distinct groups—all the substances in each group being eliminated poorly or well in a given case, as might be expected if the elimination of one group was a glomerular function, of the other group, a tubular. Instead, the elimination of each individual substance is to some degree independent of all the others.

Some very suggestive observations in this connection have been published by Folin and Denis.² They studied a series of patients oper-

¹ Bulletin of the Johns Hopkins Hospital, 1912, xxiii, 289.

² Journal of Biological Chemistry, 1915, xxii, 321.

ated upon for malignant growths of the bladder in whom a double ureterostomy rendered possible the collection of "single kidney" urines and in whom in each case one or both kidneys had been infected and previously subjected to back pressure from the neoplasm. The comparative analysis of the urine from the two kidneys in this limited number of cases shows that the damage produced by moderate hydronephrosis complicated by pyelitis is not particularly uniform in character so far as the excretory power of the kidneys is concerned. Contrary to most previous observations they found that the capacity to eliminate nitrogenous substances is more easily or more frequently damaged than is the salt excretion. Also there was lack of correspondence in the variations in phosphate and chloride excretion. The output of creatinin and uric acid likewise did not vary together.

The findings suggest that the excretion of urine by the kidney can be divided into an unknown but considerable number of more or less independent excretions.

The view that the tubules are responsible for the major excretion of all the most important substances excreted by the kidney is not at all in conflict with the fact that the most marked impairment in the excretion of all of these substances is in the advanced stages of chronic glomerulonephritis. As pointed out last year, in the early stages of glomerulonephritis when the lesion is often confined to the glomeruli, the renal functional tests are characteristically normal.

In the advanced stages, however, when renal function is severely impaired, not only are many of the glomeruli completely obliterated but their associated tubules are atrophied and probably non-functionating and the remaining tubules are frequently at this stage degenerated.

The histological studies by MacNider upon the spontaneous glomerulonephritis of the dog are of much interest in this connection (see p. 6).

NEPHRITIS. In the study of etiology, no significant advance has been made during the past year. The evidence, however, that chronic glomerulonephritis is, in the great majority of cases, a sequel to an infection usually streptococcic or pneumococcic is continually increasing. Probably a majority of the cases of chronic glomerulonephritis first present themselves to the physician in the advanced stage when failing renal function gives rise to toxic symptoms, or when a failing cardiac musculature overstrained by the long sustained high blood-pressure gives rise to edema or dyspnea. A careful inquiry into the history will usually reveal evidence of repeated attacks of tonsillitis, rheumatic fever, pneumonia, scarlet fever or other streptococcic infection, either recently or five or six years previously, or occasionally at a greater interval of time. In an earlier detection of the insidiously developing chronic nephritis, following one of these infections, lies the greatest hope of prolonging the life of these patients.

Concerning the pathology of nephritis, much is to be learned from the

experimental studies already briefly quoted (see p. 139). Upon clinical material there is one study published during the past year by W. Ophüls,¹ being a resumé of his study of a considerable number of pathological kidneys from autopsy material. His classification follows very closely that of Vollhard and Fahr described quite fully in *PROGRESSIVE MEDICINE* last year. For the "Nephrosen" of Vollhard and Fahr, also called degenerative nephritis, Ophüls prefers the term parenchymatous nephritis, acute, subacute, or chronic, with or possibly without amyloid. "Clinically, these cases are characterized by very pronounced urinary findings (much albumin, many casts), marked edema (although very emaciated cases may remain dry), absence of hypertension and a small heart." These kidneys may show inflammatory changes, hence the use of the term nephritis by Ophüls rather than nephrosis.

Concerning the histogenesis of glomerulonephritis in general, he says: "From a study of the early cases, I have become convinced that the thrombosis and subsequent hyaline necrosis of the capillary wall precedes all other changes in the glomeruli, which is in full agreement with the opinion of previous investigators. The only difficulty in the way of assuming an infectious, embolic origin for these lesions is the fact, which I can confirm from my own experience, that in spite of the most careful search one cannot find any bacteria in these masses.

"In view of the actual finding of the bacteria in focal glomerulonephritis in which the reaction is less intense, I believe, however, that we are justified in developing the following hypothesis: In cases of chronic septicemia, the endothelium of the glomeruli gradually acquires strong bacteriolytic properties. When in such cases suddenly large numbers of the bacteria are thrown into the glomeruli, an explosive bacteriolysis takes place which liberates large amounts of bacterial toxins. These cause blood destruction resulting in hyaline thrombosis, hyaline necrosis of the wall of the capillaries and the inflammatory reaction about them.

"It is evident from our specimens that the endarteritis cannot be the direct result of the inflammatory changes in the tissues about them, because, in some cases, the arterial lesions are early and extensive, in others the inflammatory changes in the connective tissue may be far advanced and the arteries remain practically normal."

He refuses to admit the existence of the "combination form" of Vollhard and Fahr, and believes that when the glomerulonephritis is largely capsular, eventually a picture is produced exactly like that in arteriosclerosis. All cases in which one can detect definite inflammatory lesions in the glomeruli, even in a few of them only, belong, he believes, from the beginning in the group of glomerulonephritis.

¹ *Journal of the American Medical Association*, 1915, lxx, 1719.

C. Frothingham, Jr.,¹ in a study of the relation between renal functional tests and the pathological anatomy of the kidney in a series of 18 cases of chronic nephropathy, has classified his materials on histological evidence into 14 cases of chronic vascular nephritis and 4 cases of chronic glomerulonephritis. No correlation could be observed between the age, urinary findings, phthalein tests, non-protein nitrogen of the blood, or blood-pressure of these patients and the group into which the kidneys were classified. Unfortunately, no note is made, however, of the degree and extent of glomerular involvement and tubular atrophy in the individual cases as compared with the clinical findings. It seems possible that a correlation might have been observed between the functional state of the kidney and the extent of glomerular and secondarily of tubular involvement as has been noted by Volhard and Fahr and by Ophüls. The writer has been much interested in this phase of the subject. As yet his material is not sufficient to warrant definite conclusions, but it apparently supports the view that there is a definite correlation between the degree of glomerular destruction and secondary tubular atrophy seen at autopsy and the impairment of the renal functional tests during life. Probably certain of Frothingham's cases of chronic vascular nephritis with extensive glomerular change represent what Volhard and Fahr call the "Combination form," a kidney which they find giving in the later stages a functional picture indistinguishable from that of advanced chronic glomerulonephritis.

TREATMENT OF NEPHRITIS. Probably the most valuable recent summary of the treatment of nephritis and of the application of the newer methods of renal functional testing to the therapeutics of the disease is that of T. C. Janeway.² He considers chronic renal disease under a grouping into five types for purposes of treatment as follows (the parentheses are the writer's):

I. Patients in whom albumin and casts in the urine are the only evidence of disease.

(a) Instances of a healing acute lesion.

(b) Instances of postural albuminuria.

(c) The remaining cases.

II. Patients with hypertension with, or without, a trace of albumin and with slight subjective symptoms or none at all (commonly called vascular or sclerotic hypertension or cardiovascular hypertensive disease. Here, too, would fall the cases of early chronic glomerulonephritis which for a variable period, sometimes for years, may exhibit hypertension with albumin and casts in the urine as the only evidence of renal disease. Only later does impairment of the renal functional tests appear in these cases).

¹ American Journal of the Medical Sciences, 1916, cli, 72.

² Ibid., 1916, cli, 157.

III. Patients with hypertension and outspoken myocardial insufficiency.

IV. Patients whose predominant symptom is general edema without notable myocardial insufficiency (renal edema); the urine is usually highly albuminous and contains casts of all kinds. (Commonly called parenchymatous or degenerative nephritis, nephrosis or nephropathy).

V. Advanced renal insufficiency, uremic symptoms being superimposed on one of the former types.

This summary of the treatment seems to the writer so excellent that he proposes to introduce a rather full abstract of it, although even then much of it that is of value and interest is, of course, omitted. A very common form of nephritis, chronic glomerulonephritis in its earliest stages would usually be classed in Janeway's Group II and is to be treated according to the principles outlined for that group. As the disease progresses, however, there appears eventually beginning impairment of the renal function which may exhibit itself as a tendency to an increase in the blood-urea or blood-chlorides or both, a falling phthalein excretion and a tendency to polyuria and fixation of the specific gravity. At this period, for which close watch should be kept, the proper treatment includes those dietetic regulations laid down by Janeway under heading III, although, of course, in these cases there is often no myocardial insufficiency, the failing renal function being of renal origin and not from passive congestion so that the cardiac measures described under heading III are not required. It is, as a rule, the protein and salt which must be curtailed as described under heading III. Edema is not a feature of these cases and restriction of the fluid intake is, therefore, not, as a rule, necessary. Indeed, a free use of water distinctly aids in eliminating the waste products. Other eliminative measures, such as mild cathartics and occasional sweating are probably beneficial. By proper use of these measures the progression to the final stage represented in Janeway's fifth group may be materially delayed. An abstract of Janeway's suggestions follows:

Chronic renal disease presents an endless variety of symptom combinations, but certain clinical types occur with such frequency as to present themselves in a way as specific practical problems:

I. *Patients in whom albumin and casts in the urine are the only evidence of disease.* One must first endeavor to single out of this group cases that are:

(a) Instances of a healing renal lesion and

(b) Instances of postural albuminuria, a condition especially common in children. Evidence that the condition is a healing renal lesion may be obtained in the form of a history of recent mild infection, tonsillitis, a recent pregnancy, syphilis, some intoxication or an administration of salvarsan. If such a possible cause can be established, especially in the case of young people, a period of rest in bed upon a milk or other bland

diet should be given a thorough trial. If this treatment results in a subsidence of the albuminuria, it should be persisted in, as in a case of acute nephritis. If, however, there is no suspicion of a past or existing infection, or if a week in bed on milk diet has no appreciable effect in diminishing the albumin and casts, so rigid a régime is probably useless, and, instead, one must search for possible foci of infection or toxemia as suggested below.

For the recognition of postural albuminuria which is to be considered especially in children (and young adults), the testing of urine passed at different times of the day, and of the urine passed after standing fifteen to thirty minutes in a markedly lordotic position, is of value, and will often clear up the diagnosis promptly. The larger amount of protein precipitable by acetic acid in the cold, has been in Janeway's experiment an important feature of the albuminous urine in these cases. (It must be remembered that not only albumin, but also casts, usually few in number and either hyaline or pale granular in type, may occur in these cases.) The treatment of these cases should, he believes, be along lines of general invigoration with medical gymnastics for the improvement of posture. The diet should be simple, not restricted. In some, the suspicion of a coexisting true nephritis is strong (the phthalein test would probably be of value in this connection, since in the postural cases it has been found to be normal). (Compare, however, the studies of Hempelmann, p. 142.)

After distinguishing the cases in the subgroups (a) and (b), there remains a large number of patients in this Group I, in whom the cause of the albuminuria is not evident. Among the causative factors to be searched for in these cases are inflammatory conditions along the urinary tract, calculus and neoplasm; a remote infection, in for example, the tonsils, gall-bladder, prostate or seminal vesicles; a toxic cause, such as arsenic, inorganic poisons (or pronounced gastro-intestinal catarrh or intestinal fermentation or putrefaction). Excessive exercise and cold baths are possible causes.

Failing to find a cause, simple albuminuria and casts are an indication for close and continued observation of the patient, with the use from time to time of one or more of the methods of functional testing. However, until increase of blood-pressure, nocturnal polyuria, fixation of the specific gravity, reduction of the phthalein output, abnormal response to the renal test-meal, or increase of the non-protein nitrogen or urea of the blood occurs, such cases demand no other treatment, except a safeguarding treatment for the protection of the kidneys against unnecessary strain. This may be outlined as follows: Avoidance of:

1. Excessive physical strain (such as competitive athletics and rough hunting trips).
2. Exposure to cold and wet.
3. Alcoholic excesses or immoderate use of tobacco.

4. Condiments, such as pepper, mustard, and spices, which are renal irritants.

5. Foods rich in creatinin and poor in nutritive value, such as meat-stock soups and broths.

6. Overeating, regardless of the type of food.

7. The use of salt, except in extreme moderation.

II. *Patients with hypertension, with or without a trace of albumin and with slight subjective symptoms or none at all* (these are the cases classed commonly as vascular or sclerotic hypertension or cardiovascular hypertensive disease). For these cases, a safe-guarding treatment is the entire problem of their management, it includes

1. The avoidance of influences which normally raise the blood-pressure, especially emotional or mental strain.

2. Securing adequate sleep, and if possible, with a mid-day rest.

3. Moderation in the use of tobacco, watching the effect on the blood-pressure.

4. Moderation or abstinence from alcohol according to the case.

5. Avoidance of excessive exertion or athletic activities. Employment of regulated exercise, but never to the point of causing anginoid pain. When exercise cannot be allowed, massage is useful.

6. Limitation of diet, including condiments, creatinin and salt, as in Group I, with particular avoidance of overeating. Meat is not necessarily to be excluded.

7. Preferably residence in winter away from cold high winds. A long break in work, once or twice a year is very helpful.

8. Turkish baths or sweating benefit some.

9. Vasodilator drugs are to be avoided, except in emergencies, and aconite, he believes, is worthless.

III. *Patients with hypertension and out-spoken myocardial insufficiency.* One of the largest groups. They require both the safe-guarding treatment of Group II and in addition, symptomatic treatment for the dyspnea, edema and chronic passive congestion of the viscera. A small number have anginoid pain or severe attacks of angina on exertion. These cases should never be permitted to indulge in enough exertion to excite an attack. To ward off an attack, fresh nitroglycerin tablets dissolved on the tongue and not swallowed, fulfil the indications. Theobromine may be valuable in some such cases.

The cases with ordinary myocardial failure require rest in bed or if orthopneic, better in a chair. If they show auricular fibrillation, they must be adequately digitalized and kept permanently under the drug. If not fibrillating, but with marked edema and congestion of the liver, they will usually be helped by digitalis, but in such cases, this drug must be more cautiously used.

Regulation of diet is one of the most essential features of treatment, the three factors to be considered being: the fluid, the salt and the

nitrogen intake. It is very important to have the fluid intake and urine output accurately measured, and it is helpful to have the daily weight recorded. Their behavior toward water, salt and nitrogen may be determined at the outset by means of a renal functional test-meal, such as that of Mosenthal, a phthalein test should be done, and, if possible, especially if the test-meal shows a lowering in the nitrogen concentration of the urine or a lag in nitrogen excretion, a determination of the blood-urea and possibly the Ambard coefficient. The most distinctive result of the test-meal in myocardial insufficiency without renal involvement other than chronic passive congestion is a low water output with a fairly high specific gravity, nearly always 1.020, extremely low salt concentration and total output, and, in contrast, a normal urea excretion brought about by the high concentration of this substance in the urine. As the degree of accompanying contraction of the kidney, becomes greater, the specific gravity tends to become fixed and at a low level, nocturnal polyuria to become marked and the concentration of the nitrogen, especially in the night urine, tends to fall far below the normal. A blood-urea above the normal or a high Ambard coefficient indicates the need for limitation of the protein intake. A satisfactory low protein diet devised by Mosenthal follows:

BREAKFAST:

Sherry, 30 c.c.

Baked apple, stewed prunes, orange.

"Hominy cornstarch cereal" (two-thirds hominy, one-third cornstarch, cream, 15 c.c.).

DINNER:

Sherry, 30 c.c.

Potato, baked or mashed, string beans, carrots, lettuce, onions, tomatoes or cucumber pickles. Fruit, cornstarch pudding or fruit tapioca pudding.

SUPPER:

Same as dinner (sugar and butter may be used as desired, and need not be weighed).

Failure to eliminate salt makes essential the reduction of the salt intake to a figure below the twenty-four output. Where much edema exists, a rigorous salt-poor diet containing less than 3 grams, if possible getting down to 1 gram, is most desirable at the start. Since these patients with myocardial insufficiency and marked edema require strict limitation of fluid as well, the Karell diet is ideal. This consists of 800 c.c. of milk in the twenty-fours as the only food or fluid allowed. Disappearance of edema usually begins after two or three days and may be little short of magical. When diuresis is abundant, the amount of milk can be gradually increased to 1500 c.c. and then the other appropriate foods gradually added. All such patients should be warned against the abuse of salt for the future, and must never take large volumes of fluid or bulky meals.

After recovery from the urgent symptoms, the return to physical activity must be by very gradual stages and carefully supervised. Massage, resistance movements, and hydrotherapeutic procedures are all helpful. The safe-guarding treatment must be rigidly maintained.

IV. *General edema without notable myocardial insufficiency* the prominent symptom; the urine usually highly albuminous and containing casts of all kinds.

This is a small group and is what has been variously called chronic degenerative nephritis or nephrosis. Elevation of blood-pressure is usually wanting. Some of these patients are found at autopsy to have amyloid kidney.

These cases exhibit disturbance of the salt and water eliminating function. The phthalein test, nitrogen elimination and blood-urea may be normal.

Treatment should always begin by a period of very low salt and water intake to promote rapid absorption of the dropsical effusions. When this has been accomplished, the fluid intake may be gradually increased, but not exceeding the capacity for excretion. Later, the salt-content may also be gradually increased, but not exceeding the capacity for excretion. Bed is desirable until normal function is restored. The further treatment is as in Group I, search for foci of infection or intoxication and safe-guarding the kidneys.

Patients with very low salt outputs and obstinate edema require accessory dehydrating measures, of which the most effective is sweating. Purging may be of some value.

V. *Advanced renal insufficiency*, uremic symptoms being superimposed on one of the former types.

All the evidences of impaired renal function are developed. The use of such a nephritic test-meal as Mosenthal's would be by virtue of its protein content objectionable in such cases. Both chloride and nitrogen excretion are impaired, but water elimination may remain intact and there may be no edema in spite of the chloride retention. The reduction of the phthalein and the increase of the blood-urea or the Ambard coefficient are of diagnostic and prognostic value in these cases.

Treatment is purely symptomatic and unfortunately often ineffectual. Dyspnea and the associated insomnia may be relieved by keeping the patient on a chair instead of in bed. Sodium nitrite at bedtime, or choral in 5- or 10-grain doses, with, or without, bromides may secure sleep. There are evidences of acidosis associated with the dyspnea, but alkali usually fails to relieve the latter symptom. Morphine may be necessary and is sometimes quite effective but, once begun, it must be continued in increasing doses and occasionally it precipitates rapid onset of anuria with coma. For gastro-intestinal disturbances, lavage of the stomach and bowel may be tried, but are often ineffectual. Diet is usually reduced to a minimum by the anorexia. In the early cases,

a very low nitrogen diet, with nitrogen starvation on days of severe symptoms, is indicated, giving as much carbohydrate as possible. Janeway has had a few remarkable improvements from this treatment.

The amount of fluid should depend upon the urinary output and should be limited only by this or by the occurrence of edema. Unless contra-indicated, a liberal allowance of water should be given to promote free diuresis which favors the removal of the retained waste products.

Of direct measures to reduce the retention of poisons, bleeding takes first place, but bleeding increases the anemia, which is apt to be a feature of the intoxication. Bleeding has its greatest value in the case of sudden convulsive seizures. The removal of at least 500 to 600 c.c. of blood is regularly indicated in such seizures and recovery is common. "I have known a number of such patients to live for several years after severe convulsions." Sweating occasionally seems to benefit these patients. The most important treatment in uremic cases is of the associated myocardial insufficiency when it exists. The superposition of chronic passive congestion on moderately damaged kidneys may precipitate severe renal insufficiency. The prognosis, when myocardial insufficiency is marked, is always much better because the element of functional disturbance may be recovered from under appropriate treatment of the heart, while gradually increasing renal insufficiency due to progressive destruction of the kidney tissue must have an absolutely hopeless outlook.

Of equal importance, but less generally appreciated, is the urgent necessity for the treatment of any associated obstruction of the urinary tract. Back pressure from an enlarged prostate with even moderate residual urine, combined with an only slightly damaged kidney, may rapidly lead to severe renal insufficiency. Pyelitis and pyelonephritis may produce similar pictures.

Janeway alludes to the probable value of decapsulation of the kidney in selected cases of nephritis, especially in cases of acute anuria or extreme oliguria. S. Wilk¹ has reported favorable results in four soldiers with trench nephritis in whom persistent edema of months' duration was rapidly relieved following decapsulation of one kidney. The kidney was found two to three times its normal size, it was bluish, and bled copiously when decapsulated. E. Meyer² reports a woman with chronic parenchymatous nephritis whom a long period of salt-free diet failed to relieve of the marked edema. Simple scarification of her kidneys, however, was followed by a very pronounced diuresis, with diminution of the edema. The operation had to be repeated, however, in a week, following which a marked improvement occurred and persisted for a year.

¹ München. med. Wehnschr., 1916, lxiii, 73.

² Ibid., 1916, lxiii, 557.

H. Strauss¹ emphasizes the value of 4.5 per cent. glucose solution for enteroclysis instead of saline solutions in conditions associated with damaged kidneys demanding introduction of fluids.

A very striking study is that of W. G. Smillie² upon the possibility of *potassium poisoning in nephritic individuals*. He observed that some nephritics upon taking 10 grams of potassium chloride exhibited symptoms of acute potassium poisoning as evidenced by prostration, precordial pain, vomiting, cyanosis and hemoglobinuria, although a normal individual could take a much larger dose without any deleterious effect. He further showed that rabbits with uranum nephritis of a degree sufficient to increase the blood non-protein nitrogen to 100 mg. per 100 c.c., die with great suddenness following the ingestion of 1 gm. of potassium chloride. This acute poisoning occurs because the salt which is normally readily absorbed but very rapidly excreted, in nephritis is readily absorbed and poorly excreted, thus reaching a concentration in the blood which is injurious.

In view of the frequent use of potassium citrate, acetate and tartrate as diuretics in nephritis, the importance of this finding seems very considerable. Care should certainly be taken not to continue the administration of these drugs in nephritis over a sufficient period to permit the accumulation of a toxic amount in the body unless an adequate elimination can be demonstrated. The corresponding sodium salts might more safely be used. In the treatment of bichloride poisoning recently suggested by S. W. Lambert and H. S. Patterson³ the continuous administration of very large doses of potassium salts is advocated. In view of Smillie's findings, it would certainly seem safer to employ the corresponding sodium salts. Lambert and Patterson's treatment is as follows:

"The first indication is to give the patient the whites of several eggs and then wash out the stomach thoroughly. This has usually been done before the patients are admitted to the hospital. On admission, the stomach contents are expressed and examined for mercury, the stomach is thoroughly washed, and a pint of milk introduced. If no stomach contents are obtained before lavage, then the lavage water is examined for mercury. Urine passed spontaneously, or that obtained by catheter, is examined for mercury. The metal appears in the urine in from three to twenty-four hours after it has been swallowed. If more than a day has elapsed since the poisoning occurred, a stool should also be examined for the poison. If the first lavage does not allay the nausea and vomiting, it is repeated after an hour, and the following routine is begun as soon as the stomach will permit:

"1. The patient is given every other hour, 8 ounces of the follow-

¹ Therap. d. Gegenwart., 1915, lvi, 361.

² Archives of Internal Medicine, 1915, xvi, 330.

³ Ibid., 1915, xvi, 865.

ing mixture: Potassium bitartrate, 1 dram; sugar, 1 dram; lactose, 1 ounce; lemon juice, 1 ounce; boiled water, 16 ounces. Eight ounces of milk are administered every alternate hour.

"2. The drop method of rectal irrigation with a solution of potassium acetate, a dram to the pint, is given continuously. The amounts of urine secreted under this treatment are very large. Two hundred and sixty-nine ounces were passed in one case in twenty-four hours on the fourteenth day of treatment.

"3. The stomach is washed out twice daily.

"4. The colon is irrigated twice daily, in order to wash out whatever poison has been eliminated in that way.

"5. The patient is given a daily sweat bath in a hot pack.

"It is imperative to emphasize the necessity of keeping up the treatment with the colonic drip enteroclysis day and night without interruption. It entails discomfort for the patient, but the victims of accidental poisoning are always willing to do anything to recover from their plight, and the attempted suicide usually repents rapidly of his error, and the hope of his life being saved stimulates his patience and desire to coöperate.

"In cases in which one single dose has been taken, after two negative examinations of the urine, on successive days, it seems legitimate to stop the treatment. In another case the urine was found to contain no mercury on at least two examinations before discharge. In view of the behavior of subsequent cases, which have been more thoroughly studied, it is probable that this patient excreted mercury for some time after leaving the hospital. For the less severe cases, a week may be sufficient time for treatment. When large or successive doses have been taken, or when there is a preëxisting kidney lesion, or when treatment begins several days after the poison is taken, longer periods of treatment, up to three weeks are necessary."

A study of *diuresis* in their hospital patients has been reported by Christian, Frothingham, O'Hare and Woods.¹ The study was based upon the routine records in the medical service of the Peter Bent Brigham Hospital of the daily total intake and urine output of a series of 600 successive patients. Any patient in whom the urine output in twenty-four hours was 1600 c.c. or over was regarded as having diuresis; furthermore, any patient in whom the urine output in twenty-four hours exceeded the fluid intake was considered to have a diuresis. They found that diuresis in this sense is relatively infrequent in the average hospital patient. Of those exhibiting it, the largest group were cases of chronic cardiac disease with decompensation, in which, with digitalis, limitation of fluid intake and rest, diuresis followed. In at least some of these cardiac cases with edema, caffeine diuretics given in connection with

¹ Am. Jour. Med. Sci., 1915, cl., 655.

digitalis, produced diuresis when the latter alone did not. In one case, theocin in connection with digitalis produced a marked diuresis, though theobromin sodium salicylate did not; the same difference was observed in this case whether the drugs were given by mouth or intravenously.

The next largest group exhibiting diuresis were the cases of chronic nephritis. A series of 100 consecutive cases with chronic nephritis that had remained in the hospital not less than one week were examined. Almost all of these cases had hypertension, and 47 of them showed evidence of a cardiac lesion, either chronic myocarditis or a chronic valvular lesion. Of the 100 cases, 43 received no diuretic therapy (increased fluid intake, digitalis, theocin or similar drugs), and of these, 12 showed a diuresis, while 31 did not. Twenty-nine patients received digitalis; 17 (of which 16 showed a cardiac lesion or cardiac decompensation) with ensuing diuresis, 12 without diuresis. In 8 patients a large fluid intake, because of thirst, caused diuresis. In 3, sodium bicarbonate appeared to cause diuresis. In 4 patients on a test-diet, diuresis occurred when either 10 grams of sodium chloride or 20 grams of urea were added to the diet.

Particularly interesting are 10 cases in which such diuretic drugs as theobromin sodium salicylate, potassium citrate, caffein and theocin produced no diuresis. Curiously enough, these so-called diuretic drugs failed very generally to produce diuresis when used alone. Most of the patients in this group had slight, if any, edema. Possibly this is the cause of so many failures to obtain diuresis in cases without cardiac failure. If so, then diuretic drugs would seem to have little value as eliminants of toxic substances in chronic nephritis without edema. Further evidence certainly is needed on this point to justify the use of diuretics in uremic conditions without edema in view of the evidence which has been accumulated that the diseased kidney is abnormally sensitive to fatigue and that diuretics may cause fatigue and consequent decrease in renal excretion. Indeed, these diuretic drugs did not have any very constant effect, even in cases of nephritis, with edema but without cardiac decompensation.

M. S. Fine and A. F. Chase¹ have shown that atophan is much less effective in increasing the excretion of uric acid when the kidneys are diseased and exhibit impaired function. The renal cells fail to respond to the stimulant.

D. J. Cameron² has noted the improvement in renal function as shown by repeated phthalein tests and blood-urea determination in cases with prostatic hypertrophy following the use of an indwelling catheter.

An observation of H. Zondek's³ in studying nephritis in children has an important bearing upon the treatment of nephritis with impaired

¹ Archives of Internal Medicine, 1915, xvi, 481.

² Journal of the American Medical Association, 1916, lxvi, 1765.

³ Ztschr. f. klin. Med., 1915, lxxxii, 14.

renal function. He has observed that frequently in nephritis the elimination of chlorides and of nitrogen in the urine have each an effect on the other, so that it is possible for the kidney to exhibit a better elimination of nitrogenous substances if the salt intake be reduced or of chlorides, if the nitrogenous intake be reduced. This possibility deserves further study to determine in what type of nephritis and to what extent it is true.

TRENCH NEPHRITIS. During the spring of 1915, there was noticed at the war front a rapidly increasing incidence of a somewhat peculiar type of acute nephritis among the British and French troops. This condition has been described during the last year by a number of writers, among whom may be mentioned J. Rose Bradford¹ and M. Gand and P. Mauriac.²

Prodromal symptoms of three to six days' duration, consisting of lassitude, headache, and lumbar pain frequently preceded the onset of the characteristic picture. This consists of a rapidly increasing edema, developing within the course of a few hours, first in the face (or occasionally in the feet) and extending over the whole body and involving the serous cavities. Dyspnea also of sudden onset may be a pronounced symptom. There is fever at first, high blood-pressure, much albuminuria, casts, and traces of blood in the urine. The most striking peculiarity is the transitory duration of the dropsy, in some instances only two or three days, in a very large proportion of cases less than ten days. The albuminuria, however, is more persistent.

Even in very severe cases, it is most exceptional for death to take place. Only three fatal cases have been seen by Bradford and one was superimposed on chronic Bright's disease, the other two, on congenitally mal-formed kidneys. Uremic complications of varying degrees are common.

Eye-ground examinations made in a few cases by Bradford, showed no changes, except where there had been a previous chronic renal disease.

Moore,³ out of 119 soldiers with epidemic nephritis, found 5 cases with renal retinitis and 7 with small retinal hemorrhages; 107 had normal eye-grounds.

The etiology of this nephritis has remained unsettled. Among the various suggestions are prolonged exposure to cold and wet, an infection streptococcic or otherwise, transmitted in the form of a tonsillitis or bronchitis, an obscure epidemic infection of which the nephritis is the only evidence, a toxic nephritis arising from some peculiarity of the food or water supply or as suggested by C. P. White⁴ from the lead and tin in the solder of tinned foods. No explanation advanced has proved

¹ Quarterly Journal of Medicine, 1916, ix, 125.

² Paris Méd., 1916, vi, 3774; Journal of the American Medical Association, 1916, lxiv, 752.

³ Lancet, 1915, ii, 1331.

⁴ Lancet, 1916, i, 996.

satisfactory. One of the most striking features was that in the Expeditionary Force, the condition was confined to the British troops, as it did not occur in the Indian troops.

RENAL TUBERCULOSIS. An excellent study of the end-results of 70 cases of renal tuberculosis treated by nephrectomy has been published during the year by E. G. Crabtree,¹ with an introduction by Hugh Cabot. The study represents the results of following up all of the cases possible from the clinic from the establishment of nephrectomy as a routine treatment for renal tuberculosis up to December, 1912. Thus all cases had been operated upon two years or more prior to the investigation. In 70 cases, definite data more or less complete were obtained. The average duration since operation was 5.6 years. The longest interval was eighteen years. Cases were evenly distributed between the sexes, but of the unimproved cases 8 out of 9 were males and of the late deaths, the deaths occurring subsequent to temporary recovery from operation, 11 out of 14 were males. This supports Wildbolz's statement that among women there is a larger percentage of cures. In ages, the cases ranged from fourteen to sixty-five years, but 58.5 per cent. occurred between twenty and forty years. In the 4 cases in which the patients were over fifty years of age the lesions were calcareous kidneys with autonephrectomies. Right-sided lesions predominated. The duration of symptoms before operation ranged from three weeks to ten years. Of the 70 cases only 24 claimed the benefits of operation before one year from the date of appearance of symptoms.

The presenting symptom, *i. e.*, the symptom which first brought to mind the fact that there was some abnormality of the body, shows that bladder irritation was by far the commonest of early symptoms, with pain in the kidney region on the affected side second. Below is given a table of the relative frequency of the presenting symptoms:

	No. of cases.	Per cent.
Bladder symptoms (bladder pain, frequency, burning, tenesmus, etc.)	34	48.5
Pain in the kidney region	25	35.7
Loss of weight and strength	3	
Pain in penis on micturition	2	
Hematuria without any other symptom for a time	3	
Chills and fever with pyuria (complicated tubercu- losis)	1	
Referred pain (colic) associated with hematuria	1	
Acute retention from pus and blood clot	1	

The data available indicate that pain in the kidney region, whether occurring as presenting symptom or in the course of the disease, is of

¹ Surgery, Gynecology and Obstetrics, 1915, xxi, 669.

dull, aching character, situated in the costovertebral angle or indefinitely located in the affected side, except in the few cases in which there is hemorrhage with the passage of blood-clot down the ureter, in which cases the character of the pain becomes colicky and is localized and referred as in ureteral calculus. There were no cases of crossed pain, *i. e.*, referred to the unaffected kidney.

In two-thirds of the cases, the temperature fluctuated irregularly between normal and 100° . In 2 cases with secondary infection, the temperature rose from 102° to 104° and remained so until operation, over a period of five and seven days respectively. In 20 of the cases, the temperature was normal.

87.1 per cent. of the cases showed from a trace to the very slightest possible trace of albumin. The sediment showed pus in 60 (85.7 per cent.) of the cases and microscopic blood in 33 (41.4 per cent.). Twelve other cases gave a satisfactory history of having passed blood at some time since the onset of symptoms.

18.5 per cent. in the series showed definite clinical, and, in some cases x-ray, evidence of pulmonary consolidation with or without evidence of activity of the process, or gave a history of unexplained pleurisy.

Tuberculosis of the epididymis was found previous to operation in 3 cases. Prostatic tuberculosis, tuberculosis of the knee, tuberculous adenitis in the neck, and tuberculous stricture of the ureter were each observed in a few cases.

Curiously enough in comparing the type and extent of lesion found on removing the kidney with the outcome of the case, it is found that in extensive tuberculous involvement, even in the tuberculous pyonephrosis, recovery is the rule, while in early tuberculosis the percentage of cured cases is low.

The immediate mortality following operation was 4 cases out of 103. Out of 70 cases, 14 had died of tuberculosis subsequent to temporary recovery from operation. Four died within three months, from tuberculous cachexia. Half of the 14 died during the first year, the other 7 at an average of 3.3 years. Both meningitis and miliary tuberculosis are more frequently met with in genito-urinary tuberculosis than in other forms of the disease.

Frequency was still a complaint in 24 cases although in the great majority it had greatly improved by the end of two years. The great majority of cases in which there was little or no improvement at the end of two years continued to have troublesome symptoms indefinitely. Few patients have made noteworthy improvement after four years. All cases now living report either a temporary or permanent gain in weight and improvement in general health. The great majority have maintained the greater part of their gain.

"We have classified as 'cured' those patients in good general physical condition; with maintained gain in weight; without evidence of exten-

sion of the disease, or if new foci have developed they are now quiescent; with improvement of bladder symptoms and no evidence of active lesions in the genito-urinary tract. Sixty per cent. of the cases in the series conform to these requirements."

"The term 'unimproved' is applied to those patients who may or may not have maintained their postoperative gain in weight; whose general physical condition is below normal; who still have active secondary lesions of the genito-urinary or in whom the disease progressed and the new lesions are active; and in whom nephrectomy has not afforded the expected retardation of the disease; 12.8 per cent. of the cases are unimproved."

GENITO-URINARY DISEASES.

By CHARLES W. BONNEY, M.D.

THE KIDNEYS, URETERS AND BLADDER.

Renal and Ureteral Calculi. During the past year, three interesting contributions to this subject have been made by Hugh Cabot,¹ of Boston. In one, he presents an analysis of 157 cases which were treated in the Massachusetts General Hospital from January 1, 1907, to January 1, 1914. Of these cases, 108 were in men and 46 in women. A study of the age incidence showed that the greatest number of patients came to operation between the ages of twenty and forty, and a considerable number between forty and fifty, although the trouble in many instances began during the first and second decades, the largest number being between the second and third decades; thus, there were 56 patients who first developed symptoms during this period. The right side was more frequently affected in women and the left side in men, a circumstance which strengthens the theory that mobility of the right kidney, which is more common in women, may be an etiological factor, in that it leads to retention of urine in the renal pelvis with resulting deposition of urinary salts and the formation of calculi.

The analysis of symptoms is interesting: In 50 cases renal colic was the most prominent symptom, and in 46 others there was occasional sharp pain referable to the lumbar region. Its relative unimportance in these cases, however, was shown by the fact that a history of its occurrence was frequently elicited only by careful interrogation of the patient. Other important symptoms were dull pain in the lumbar region, which was present in 32 cases; pain referred to the bladder in 7; backache in 8.

With reference to the urinary analysis, there were 21 cases in which the urine was normal, and, of this number, 15 were cases of ureteral calculus and 6 of renal stone. Thus it seems that there is greater likelihood of obtaining a normal urine report when there is a stone in the ureter than when one is lodged in the kidney. X-ray plates, or reports based upon the same, were available in 127 of the cases, out of which number 8 were persistently negative.

Cabot believes that this percentage, namely, 6 per cent., does not accurately represent the actual percentage of the failure of the rays to show a calculus, and expresses the opinion that 15 per cent. would be

¹ Journal of American Medical Association, October 9, 1915.

more accurate, even in the hands of the most skilful radiographers. In Mayo's¹ series of cases, the *x*-rays were negative in 11 per cent. One hundred and forty operations were performed. Out of this number there were 5 deaths, 2 following nephrectomy, and 1 each occurring after pyelotomy, ureterotomy, and nephrotomy. Nephrectomy was done 20 times; pyelotomy, 47; ureterotomy, 36; and nephrotomy 37 times. A considerable number of the nephrectomies were performed upon patients who had been treated during the earlier years of the period.

The author has come to consider pyelotomy the operation of choice in all cases in which the stone can be removed through the renal pelvis.

As to the results of operative treatment, 85 patients were examined more than two years after the operation with reference to their general physical condition, the condition of the urine, and the condition of the kidney, as shown by the *x*-rays. Those who showed normal urine and a negative radiograph were considered well. In this class were 33 who had had renal and 15 who had had ureteral stones removed.

One of the most interesting portions of Cabot's paper is that which he devotes to a consideration of the unnecessary operations which had been done in this series of cases. Out of this number, there were 26 patients who had undergone abdominal operations without relief of the symptoms.

In a second contribution dealing with this aspect of the subject, the author² discusses in detail the errors in diagnosis which led to the performance of the previous operations. An examination of the record of these surgical procedures shows that the appendix was removed in 10 cases; that is, in almost one-half of the total number. This coincides with the experience frequently reported by various surgeons, of the unnecessary and useless removal of this vestigial organ for symptoms depending upon calculous disease in the upper portion of the urinary tract. There were also 8 cases of exploratory laparotomy, and 4 in which a presumably movable kidney was anchored in position. There was one operation for gall-stones; one for imaginary adhesions; one for removal of tube and ovary; one in which the kidney was decapsulated, and one which Cabot characterizes as the "crowning iniquity," namely, "suprapubic cystotomy in a normal bladder for stone which was situated more than two feet away."

Inasmuch as these blunders were made by those whom the author designates as "reasonably competent surgeons," he was led to investigate, as thoroughly as possible, how such mistakes had happened. It was found that abdominal pain, which, however, was not spasmodic, and in no way resembled colic, was the most prominent symptom in 13 cases; that pain in the right lower quadrant of the abdomen was the most pronounced symptom in 12 cases; and that backache was the most

¹ Braasch, *Journal of American Medical Association*, 1915, vol. lxxv.

² *Surgery, Gynecology and Obstetrics*, October, 1915.

prominent symptom in 11 cases. In this group of 36 cases the pain was not at all characteristic of calculus, and might have been mistaken for that which is associated with a variety of abdominal diseases. Attention is called to the surprising, though not uncommon, diagnosis of Bright's disease in cases of calculus in which abnormal urine is the most prominent or even the only symptom.

An interesting class of cases is that in which backache, particularly pain in the region of the sacroiliac joint, is the chief complaint. A number of such cases, it is stated, are referred every year from the orthopedic department. These are the ones in which error could be most easily avoided, it seems to me, if further examination of the patient's condition were made; for urine examination, the use of the *x*-rays and the ureteral catheter should readily clear up the diagnosis. It seems strange also that such symptoms as difficult or painful urination should not arouse a suspicion of trouble high in the urinary tract when nothing low down could be found to explain it. It has been my experience to have cases of this kind, however, and only recently a man was brought to me for stricture of the urethra who had had attacks of renal colic off and on for seventeen years. The stricture from which he was suffering was unquestionably traumatic, caused by laceration of the urethra during the passage of the calculi.

In Cabot's cases, there were some in which a diagnosis of neurasthenia had been made. The patients had complained of abdominal pain, but had not shown any abnormality of the urine, and were apparently negative as to physical examination. Two such patients were cured of their neurasthenia by the removal of stones.

Returning to a discussion of the *x*-rays in the diagnosis of renal and ureteral calculi, Cabot dwells at length upon those cases in which a "doubtful shadow" is reported, and is not inclined to attribute the slightest importance to such a report, be it "probably positive" or "probably negative." He remarks that the "probability" seems to depend more upon recent mistakes that the radiologist has made than upon any circumstances connected with the doubtful shadow itself.

In this connection, the experience of Eisendrath is interesting. In a paper read before the Michigan State Medical Society, he¹ emphasized the importance of using a compression apparatus to limit the movements of respiration and also to bring the *x*-ray tube into closer contact with the structures to be radiographed. He has found that both kidneys and the upper portion of both ureters can usually be taken in one picture, and that the bladder and the lower portion of the ureters can be obtained in a second one. Except in the cases of very stout persons, he believes that this method will suffice. Another point upon which much emphasis is placed is the angle at which the pictures of the bony

¹ Chicago Medical Recorder, March, 1916.

pelvis are taken. Unless the pelvis is considerably tilted, there is danger that the shadow of ureteral calculi may be obscured by parts of the sacrum or pubis. It is Eisendrath's practice to leave the cystoscope in the bladder when having a picture taken of the pelvic portion of the ureter, as he believes that the ureter is better supported in this way. He thinks that it may fall forward a little if the support of the catheter within it be lessened by taking the cystoscope out of the bladder. This method should prove especially serviceable in enabling one to differentiate between shadows produced by calculi in the pelvic portion of the ureter and those caused by calcified tuberculous lymph nodes, phleboliths, etc.

Braasch,¹ who has reported a large number of cases from the Mayo Clinic, expresses the opinion that a positive diagnosis by the x-rays alone cannot be made in more than 60 per cent. of all cases of ureteral calculi. The sources of failure in the 32 cases (11 per cent.) of the series in which the röntgenogram was negative, were, in the order of their frequency, faulty technic, position of the stone, size of the stone, and character of the stone. Braasch believes that there will always be slips in technic which will result in error. He also points out, as has been previously mentioned, that shadows of the pelvic bones may obscure the shadow of the calculus, and that it may not always be possible to adjust the angle of the ray in such a way as to overcome this difficulty. Very minute stones, too, may be overlooked in the picture, and a few are composed of substances which do not cast a shadow. After all, however, the author feels that more mistakes will be made from incorrect interpretation of the plate than from failure of the rays to show the stone.

Cabot mentions 2 cases in which calcified tuberculous glands produced obstruction and dilatation of the ureter; and, as such glands may be in close contact with any portion of the ureter, and by impinging upon it interfere with urination, he thinks that in obscure cases the possible presence of such a lesion should be considered. The use of the radiographic ureteral catheter is considered very helpful in cases of doubtful shadow, as it enables one to locate the shadow with reference to its position to the kidney and ureter. Of course, when there is obstruction to the passage of the catheter, the value of this method is greatly lessened. The wax-tipped catheter is likewise considered a valuable diagnostic adjunct.

Treatment of these doubtful cases will depend upon the degree of trouble existing in each individual case, and the author very wisely denominates as "meddlesome" any intervention not justified by the severity of the symptoms. He mentions 2 cases in which he operated in the presence of symptoms suggesting ureteral calculus but in which none was found. In one of these it was impossible to engage even the

¹ Journal of American Medical Association, 1915, vol. lxx.

tip of the catheter in the ureteral orifice, and it was taken for granted that there was obstruction higher up.

Paul M. Pilcher,¹ of Brooklyn, has presented an analysis of the cases of ureteral and renal calculi which have come under his observation during the last five years. There were 19 cases of renal calculus; 14 of calculus arrested in the ureter, and a number in which the stone was being passed at the time the patients were seen. In 5 cases of renal stone, the affection was confined entirely to one kidney, and the stones were removed by pyelotomy without any attack upon the renal parenchyma itself. In 2 cases so much destruction of the kidney had taken place that nephrectomy had to be performed. In these cases there was no mortality. In 11 cases the patient refused surgical treatment because they were not suffering to any extent, the stones being in the pelvis of the kidney. As the result of medical treatment, the stone was expelled in one case and in two others a large amount of gravel and sand was passed. Of the ureter cases, there were 9 which were treated by medicine, and in 5 of these the stones were passed. In 2 cases the calculi were removed by intravesical manipulations performed through the cystoscope, and in 2 others ureterotomy was resorted to. Ureterotomy was also performed in another case in which no medical treatment had been given, and two calculi were removed with the ureter and kidney. These 9 cases were of long duration. One patient who had had a number of stones in both kidneys, together with pyonephrosis, died from uremia after the performance of pyelolithotomy.

In discussing the use of *bismuth paste* in genito-urinary cases, Emil G. Beck,² of Chicago, states that all the cases of persistent fistula after nephrectomy that he has treated during the last eight years have been healed by the injection of this substance. He considers this condition the most favorable for the use of the paste. As it is necessary that every pocket and channel of the sinus be completely filled, the paste should be liquefied and injected under considerable pressure with a glass or metal syringe.

An interesting case of ureteral calculus in which a stone impacted 2 cm. above the ureteral orifice gave rise to no urinary disturbances, but caused constant pain which the patient referred to the internal generative organs has been reported by L. Adler.³ On vaginal examination, a small, though very hard, tumor was found about 3 cm. to the right of the uterus and somewhat anterior to that organ. Its nature being suspected, the patient was cystoscoped and an attempt made to catheterize the right ureter, the orifice of which was injected and swollen. The catheter became arrested 2 cm. above the surface. The method of removing this stone also lends interest to the case. It was taken out

¹ Long Island Medical Journal, March, 1916.

² Surgery, Gynecology and Obstetrics, May, 1916.

³ Wien. klin. Wchnschr., December 15, 1915.

through a vaginal incision in the anterior wall, the ureter being isolated and incised after the bladder had been freely pushed away from the uterus and vagina. The ureteral incision was closed, but a small gauze drain was left in the vaginal incision. The operation resulted in complete relief of the pain of which the patient had complained.

Pyelography. In a previous review, deaths after pyelography have been discussed. In a recent communication, Simmonds¹ reports a case in which fatal sepsis developed after 15 c.c. of 5 per cent. collargol solution had been injected into the right renal pelvis. There was some disturbance shortly after the injection, such as a feeling of tension deep in the lumbar region, associated with malaise and vomiting, but these symptoms had practically subsided by the next day. Toward the second evening, however, the temperature began to rise and had become very high by the morning of the third day. There was also suppression of urine and a generalized hemorrhagic eruption. A hemolytic streptococcus was recovered from the blood. Death took place on the third day. At autopsy, erosions were found in the ureter, caused in all probability by the catheterization. Through these breaks in the continuity of the mucosa it is believed that the streptococci gained entrance, although it is not known whether they came from the bladder or from the urethra.

The lessons to be learned from this case are that the greatest care should be taken to avoid the infliction of trauma during the passage of the ureteral catheter; that it is probably better to refrain from pyelography in cases in which there is any infection in the lower urinary tract; and, finally, that the bactericidal power of weak solutions of collargol is not sufficient to destroy virulent microorganisms.

Plotkin,² in reporting a series of cases from Joseph's Clinic, in Berlin, makes the point that no attempt should be made to inject the pelvis of the kidney if the passage of the catheter causes more than the usual degree of pain, or if it produces hemorrhage. In skilful hands, he considers the procedure a safe one, and compares it to a simple washing out of the pelvis of the kidney. Of course, much depends upon what one means by "skilful," and it is my opinion that only those who have been especially trained in this technic for a considerable period of time should attempt to carry it out. Cases of death reported by various authors, and which received due consideration in a previous review, together with the more recent expressions of opinion by those of wide experience in the use of the method, seem to justify this opinion.

In the 80 cases which Plotkin reports, there were 3 in which complications of considerable gravity developed. In one large hospital in Philadelphia, the surgeon-in-chief forbade the use of the method on the

¹ Med. Wehnschr., February 15, 1916.

² Journal d'Urologie, September, 1915.

ground that its potentialities for evil are too great. One patient suffered from excruciating colic immediately after the injection and had to be kept in bed for twenty-four hours. One developed high fever, with great restlessness and mental excitement, which fortunately subsided after four hours. In another case, a mild colic supervened. Great importance is attached to the use of a catheter sufficiently small to allow reflux of the fluid once the pelvis has been filled. The maximum quantity of fluid employed was 30 c.c., even in cases in which there were hydronephritic sacs, and the author recommends that this quantity be not exceeded.

S. R. Woodruff,¹ in describing his technic, states that his patients are always kept on the table for fully one-half hour after the skiagram is taken in order to facilitate the outflow of the fluid. Unless a cavity is present in the kidney, however, the catheter is removed. Woodruff injects only by gravity, holding the container in his left hand, so that the pressure can be changed instantaneously.

The experiments of Eisendrath were described in this review a few years ago. In a more recent contribution,² he particularly lays stress upon the importance of injecting the fluid under moderate pressure and states that, if the container be held at an elevation not higher than 3 feet, the fluid will not be forced into the substance of the kidney, and thence into the renal veins and general circulation. He considers the method of sufficient value in certain classes of cases to warrant its use by those who are thoroughly familiar with the technic; particularly in cases of movable kidney and intermittent hydronephrosis does he consider it of value, as it enables one to determine the range of movement of the kidney and to judge thereby whether the symptoms complained of are dependent upon its movability. He injects the renal pelvis with collargol and then has radiographs taken with the patient in the erect and horizontal postures and observes the difference in the position of the kidney in the two pictures. In addition to demonstrating the range of movement of the kidney, the author has found that pyelography will show whether there is a kink in the ureter and dilatation of the renal pelvis. It is considered valuable, too, after operation for fixation of the kidney, inasmuch as it enables the surgeon to determine whether the organ has been properly fixed and whether a kink has been produced in the ureter by the operation.

From the Brady Urological Institute of the Johns Hopkins Hospital comes the information that a solution of thorium citrate has been found to be a very satisfactory substitute for collargol as it is practically non-toxic and non-irritating, and possesses sufficient fluidity to render its escape from the pelvis of the kidney easy; moreover, it gives an excellent shadow.

¹ Surgery, Gynecology and Obstetrics, 1916, p. 241.

² Chicago Medical Recorder, March, 1916.

J. Edward Burns¹ reports very favorably upon this substance. The solution is prepared as follows: To 10 grams of thorium nitrate as much distilled water is added as is required to dissolve the salt, and then, while the solution is kept hot, 30 c.c. of a 50 per cent. solution of sodium citrate are gradually added, the mixture being shaken each time. This mixture is neutralized by the addition of normal sodium hydroxide solution, and then made up to the required volume of 100 c.c. by the addition of distilled water. The solution is filtered and then sterilized, after which it is ready for use. It contains approximately 15 per cent. of thorium nitrate, about 9 per cent. of sodium nitrate, and 21 per cent. of sodium citrate, the thorium probably being in the form of a double citrate of sodium and thorium.

In the preparation of this solution a white precipitate is formed upon the addition of the citrate of sodium solution, but it dissolves after all of the latter has been added. No evidence of irritation of the mucous membrane has been found after the use of this solution, and no urinary symptoms have been produced. Experimentally, it has been injected into the peritoneal cavity of animals, which were later killed and examined, and in no instance was there any sign of peritonitis. The non-irritating property of the solution is supposed to be due to its neutralization with sodium hydroxide, a step in its preparation to which the author attaches great importance.

Some of the animals, however, died as the result of the injection, so the substance cannot be said to be absolutely non-toxic. Immediate death also followed intravenous injection of 2.5 c.c. administered to a dog. The autopsy, however, was negative. In a series of 125 cases in which the solution was used for pyelography in quantities varying from a few cubic centimeters to almost a liter, there was not the slightest evidence of toxicity, hence it may be stated that, so far as its clinical use is concerned, the solution seems to be non-poisonous.

Lavage of the Renal Pelvis in Chronic Colon Bacillus Infection. In this form of pyelitis very satisfactory results from lavage are reported by Kretschmer and Gaarde,² of Chicago, who express the opinion that a greater number of bacteriological cures can be obtained by it, and in a shorter time, than by any other therapeutic measure. They also state that in cases of supposed pyelitis in which improvement fails to take place, one should be suspicious of some complicating condition, such as calculus, stricture of the ureter, or tuberculosis. Simple clearing up of turbid urine cannot be considered a cure, and in their series of cases no patients were discharged until cultures of the urine obtained by ureteral catheterization had become sterile. The latter desideratum, it may be readily understood, was more difficult to secure than the former. Unless cultures of the urine are negative, the danger of relapse is considerable.

¹ Bulletin of Johns Hopkins Hospital, June, 1916.

² Journal of American Medical Association, June 24, 1916

In treating this class of cases, it is also important to remove any concealed focus of infection which may later give rise to a recurrence; thus, when there is a vesical infection, treatment of the bladder must be continued until the urine shows no microorganisms; and if there be a chronic prostatitis, that likewise must receive adequate treatment. In a case of this kind cited by the authors, three recurrences took place, apparently owing to negligence on the part of the patient in having his prostatitis regularly treated.

The technic employed by the authors is as follows: As a rule a 1 per cent. solution of silver nitrate is employed, the amount injected varying from 5 to 10 c.c., with an average of from 5 to 7 c.c. Care is always taken to avoid a rapid filling of the pelvis, a point upon which the authors lay great stress. They find that the procedure is not nearly as painful when the injection is made slowly and the pelvis not overdistended. In a case in which there was an accumulation of thick pus in the pelvis, as shown by particles flowing out of the catheter, a preliminary irrigation with 30 c.c. of boric acid solution was made before the silver was injected. Small ureteral catheters were used, so that the fluid could flow out of the pelvis alongside the instrument, thereby guarding against overdistention.

Treatment was given once every five or six days until the urine was free from pus and was sterile. In about half the cases autogenous vaccines were used. For internal treatment, three drugs were employed: During the first week after the diagnosis was made one teaspoonful of bicarbonate of soda was given three times daily to render the urine alkaline. Then, during the second week, acid sodium phosphate was administered in quantity sufficient to make the urine acid, also hexamethylenamin, from 30 to 70 grains per diem. This form of internal treatment was continued during alternate weeks. Of the patients treated, 14 were followed long enough to determine whether bacteriologic cures had been obtained, and this was found to be the case in 11 of the number. In the remaining 3, although the urine was free from pus and the patients were clinically well, positive cultures were obtained from the ureters. In 4 cases, one injection was given; in 5 cases, 2; in 3, 3; in 1 case, 4, and in another, 8.

A few cases of pyelitis of pregnancy were also treated, but they are not included in this series. The authors express the opinion that lavage should be tried before interruption of pregnancy is considered, and also before nephrotomy or other operation upon the kidney is resorted to.

Gonorrheal Ureteropyelitis Treated by Antimeningococcus Serum. M. L. Boyd,¹ of Atlanta, reports 2 cases of gonorrheal ureteropyelitis treated by injections of antimeningococcus serum. One case was that

¹ Surgery, Gynecology and Obstetrics, 1915.

of a man, aged thirty-one years, who first sought advice for pain in the right lumbar region and right thigh, together with increased frequency of urination, these symptoms having developed as sequelæ of gonorrhea. About three weeks prior to the time that he first came under Boyd's observation, and when he was apparently about cured of his gonorrhea, he voided some blood after urination and experienced considerable vesical tenesmus. Ten days later, pain in the back and lower extremities developed. When first seen, he was not voiding any blood and had very little urethral discharge. The entire quantity of urine was cloudy. His temperature was 102° F. He was confined to bed, and given gonorrheal vaccines. Within a few days his temperature became normal, but rose slightly after the injection of the vaccines. As the urine did not clear up after the patient's local and general condition improved, he was cystoscoped and ureteral catheterization undertaken. The urine from the left kidney contained much pus and many gonococci. Although cloudy urine was discharged from the right ureteral orifice, it was impossible to introduce a catheter into the ureter. Later, however, this was accomplished, and urine of the same character was obtained as from the left one. After lavage with silver nitrate solution had been practised a number of times without any improvement in the patient's condition, an injection of meningococcus serum was made into the right buttock. There was very little reaction, and a larger dose was given four days later and repeated at the expiration of another five days. From the first, there was improvement in the condition of the urine, so that after the third injection it had almost entirely cleared up. After the fourth injection neither pus nor gonococci could be found.

The case of the second patient was similar, so far as the history and complications of his gonorrhea were concerned. His urine was likewise cloudy in its entirety, and contained pus cells and an abundance of gonococci. The urethra and bladder were thoroughly washed out under hydrostatic pressure, after which a soft rubber catheter was passed into the bladder and the urine collected. It was cloudy, and as there was nothing to indicate that the source of pus was the prostate or the seminal vesicles, the diagnosis of ureteropyelitis was made. Several injections of antimeningococcus serum were given during a period of about three weeks, with the result that the urine cleared up. The author gave rather small doses of this serum, varying from 5 to 15 c.c.

Ascending Lymphatic Renal Infection. In this review, some years ago, the investigations of Franke concerning the communication of the lymphatics of the ascending colon with those of the right kidney were mentioned. Since that time his ideas have been generally accepted. A preliminary report by Eisendrath and Kahn,¹ of Chicago, based upon

¹ Journal of American Medical Association, February 19, 1916.

a series of 27 experiments performed upon dogs and rabbits, seem to show that ascending infection travels to the kidneys and the perirenal tissue through the lymphatics of the ureter instead of directly along its mucous membrane. An emulsion of the usual organisms found in urinary infections was injected directly into the bladder of the animals through a sterilized ureteral catheter, some of the urine from the bladder being taken for culture before the injection was made. By this method, it was possible to avoid all injury to the bladder and ureters, and to imitate the conditions under which organisms normally travel upward from the bladder after accidental infection of that viscus has taken place.

Sections from different portions of the bladder, ureter, and kidney were examined. The ureter was also split longitudinally and sections made in this manner were likewise examined. It was found that inflammatory infiltrates had followed the course of the lymphatics. In the early stages they were seen around and within the walls of the blood-vessels in the peri-ureteral sheath. The other coats of the ureter became infected from without inward as the inflammatory process continued, the mucous lining remaining intact until all the other tunics had been involved.

Examinations of sections of the renal pelvis showed that the infiltration began in the subpelvic areolar tissue and around the blood-vessels which enter the pelvis, and that the overlying mucosa was not involved early in the morbid process. From these circumstances, the authors conclude that the lymphatics of the subpelvic areolar tissue form the link connecting the lymphatics of the ureters with those within the kidney.

In 6 out of 27 experiments, pure cultures of the same organism which had been injected into the bladder were obtained from the renal pelvis.

Six dogs were used as controls, and no evidence was found of such infiltration as was observed in the organs of the animals used for the experiments. From the rabbit controls, however, which were 12 in number, evidence of very slight infiltration was found in 5. This the authors explain by the great susceptibility of rabbits to all kinds of infection. They attribute the changes to slight ascending urinary infection which occurred accidentally.

Rupture of the Kidney. An interesting article on this subject has been contributed by F. Gregory Connell,¹ of Oshkosh, Wisconsin, who dwells at length upon the diagnosis of the condition, as well as upon its etiology and treatment. The important points to which he calls attention are the presence of hematuria, the transitory nature or even absence of shock, severe pain at the time of injury, and muscular rigidity in the region of the kidney. Hemorrhage is almost always present, although

¹ Surgery, Gynecology and Obstetrics, June, 1916.

its onset may be delayed; if the ureter is occluded by a blood clot it may be absent, as it likewise is when there is complete transverse division of the ureter or the pelvis of the kidney. The author states that in the cases which he has studied failure to recognize that shock is not an inevitable accompaniment of the injury has frequently led to mistaken diagnosis and consequent failure to institute proper treatment. He attributes little importance to tumor in the lumbar region, because it often does not develop until late after the injury, and in some cases does not occur at all. Given a history of abdominal injury associated with muscular rigidity, tenderness and hematuria, the author believes that it is justifiable to make an exploratory incision. He bases this opinion upon the circumstance that there may be no differential symptoms or signs between a slight injury and complete rupture. Therefore he feels that the welfare of the patient will be best conserved by doing an exploratory operation, although he admits that in a certain number the exposure of the kidney will have been necessary. This, he feels, will be counterbalanced by the number of deaths which will be prevented.

In discussing the investigations of Michelson and Ponomareff in this review for 1912 and 1914 respectively, the excellent results obtained by expectant treatment were clearly set forth.

In Michelson's report of 30 cases, in none of which was there surgical intervention, the mortality was only 10 per cent., and in 3 cases in which death took place there were associated injuries to other organs, so that death could not be attributed to the renal injury.

In Ponomareff's report, based upon 57 cases, there were also 3 patients who died as the result of injury to associated organs. Three left the hospital uncured; the remaining 51 made complete recoveries, and out of that number only 8 were operated upon.

In comparison with these results, Connel quotes Watson's collected series, which gives a mortality of 27 per cent. under expectant treatment, 22.5 per cent. in cases in which nephrectomy was performed, and 8.5 per cent. in cases in which drainage, with packing or suture, was employed. This latter method is the one which Connel recommends for the majority of cases, reserving nephrectomy for those in which the kidney has been seriously damaged, or for cases seen some time after the injury and in which infection has taken place. He reports 4 personal cases, 3 of which were treated by conservative operation and 1 by nephrectomy. All of the patients made good recoveries.

An interesting case of *rupture of the kidney caused by a grenade splinter* has been reported by F. Danziger.¹ It was that of a soldier who was wounded in battle. At operation, the kidney was found to be cleanly divided into two pieces. The treatment consisted in flushing out and

¹ Berl. klin. Wchnschr., 1916, liii, 160.

packing the wound after the ureter had been removed and the bleeding vessels ligated. The tampon was removed at the end of a few days and the two parts of the kidney sutured together. The patient made an excellent recovery.

Perinephric Abscess. A study of 67 cases of perinephric abscess operated upon at the Mayo Clinic has been made by W. F. Braasch.¹ The causes upon which they depended were classified, in the order of their frequency, under the headings of pyonephrosis, renal tuberculosis, renal calculus, suppuration in the cortex of the kidney and traumatism. Twice as many men were affected as women. In 18 patients no evidence of disease of the kidney could be found upon clinical examination. The author attaches considerable importance to the etiological influence of small cortical or subcapsular collections of pus, which he believes were the cause of a number of obscure cases. As a matter of differential diagnosis, he lays great stress upon the importance of careful microscopic and bacteriological examination of the urine, both that obtained from the bladder and specimens obtained separately from each kidney by catheterization of the ureters. This method enables one to determine whether there is infection within the renal pelvis. The x-ray is also considered a valuable differential diagnostic measure.

Of the 67 patients, 2 died shortly after operation and 3 within three months thereafter. In 18, the wound healed within a month; in 25, it continued to drain from two to six months, and, in 4, the fistula had not closed up to the time that the cases were reported.

With reference to treatment, Braasch believes that drainage will meet all the indications when there is a large fluctuating abscess and the patient is weak and exhausted. If there is much destruction of the kidney tissue, however, he advises evacuation of the pus followed by nephrectomy and free drainage. Of course, in such cases it is necessary to determine the functional capacity of both kidneys, and this is one of the measures which Braasch recommends.

Kidney Decapsulation. Four cases of nephritis treated by decapsulation are reported by Wilk. All were in German soldiers who had seen active military service. With the exception of severe manifestations of renal insufficiency, there seemed to be nothing wrong with them. All were edematous; their urine was diminished in quantity, was alkaline, and contained casts and a few red blood corpuscles. A functional test showed a considerable diminution of elimination. Medical treatment proving futile, a decapsulation operation was decided upon. One kidney only was decapsulated. In each case there was considerable perirenal inflammation and the kidney was also much larger than normal. Improvement followed the operation very quickly, the edema diminishing and the output of urine becoming more

¹ California State Journal of Medicine, January, 1916.

abundant from the first. Although the cortex of the kidney was very much congested and bleeding was free during the operation, the post-operative hematuria lasted only a few days. At the expiration of three weeks there were only faint traces of albumin in the urine. The author recommends this operation in cases in which medical treatment has failed, and especially in the cases of soldiers who may become ill during the war. This operation was fully discussed some years ago, so no further comments will be made upon it at this time.

Renal Tuberculosis. At the last meeting of the New York State Medical Society, Henry D. Furniss¹ reported 33 cases of renal tuberculosis which had come under his personal observation. In 50 per cent. of these cases cystitis was the first symptom, and in 15 per cent. microscopic hematuria was followed by cystitis. Renal or ureteral colic also occurred in 15 per cent. of the cases. At the time they applied for treatment, almost all of the patients had gross lesions in the bladder, consisting of edema and congestion of the ureteral orifice, and in many cases of distinct nodular infiltrations in this region. In later cases, ulcerations were observed; in some of very long duration, large areas of the bladder wall were involved. In 85 per cent. of the cases, tubercle bacilli were found in smears prepared from the centrifugalized urine. The majority of the patients had suffered no impairment of the general health. Treatment consisted in removing the kidney. There was only one operative death, and that in a case in which the lungs also were tuberculous. In about 30 per cent. there were fistulas. With reference to postoperative fistula, the author stated that its incidence was about the same whether or not drainage was used, although it might have been a little lower in the undrained cases. When excision of the ureter was required, it was performed through an extra incision. After the operation, typical tuberculin reaction was obtained; there was also an exacerbation of any associated tuberculous processes, together with increased temperature. The patients varied in age from twenty to thirty. Twenty per cent. of them gave a history of other forms of tuberculosis, 15 per cent. of the number having associated pulmonary disease.

Arthur H. Curtis,² of Chicago, in discussing laboratory methods of diagnosing chronic urinary infections, suggests the following method for obscure cases of pyuria in which tuberculosis is suspected: He begins by administering potassium iodide for a period of several days provided, of course, that there are no suspicious pulmonary signs. Then 0.1 mg. of old tuberculin is injected every twenty-four to forty-eight hours before the urinary examination. The quantity of liquids is reduced to the minimum so as to produce irritation of the kidney by concentration of the urine and also to increase the number of bacteria

¹ Journal of American Medical Association, June 24, 1916.

² International Journal of Surgery, January, 1916.

in a given quantity voided. Massage of the kidneys is also practised several times a day for a few days prior to the examination. The specimens are centrifugalized in a high-power centrifuge which the author believes to be much better than those ordinarily used. Specimens of the sediment are stained and injected into guinea-pigs, and Petroff cultures likewise made. The author believes that there is a tendency to attach too much importance to functional urinary tests at the expense of careful bacteriological examinations.

Renal Tumors. *HYPERNEPHIOMA* is recognized as one of the most fatal of renal neoplasms owing to the great frequency with which metastases occur in the lungs and liver and in the osseous and lymphatic systems, and also because of involvement of the contiguous parts by direct extension of the neoplastic growth. The late Edgar Gareau, in a study of 32 cases, found that the average duration of the disease from its first manifestation to the time when it caused death was three and a half years. Cases have been reported, however, in which a much longer time elapsed between the onset of symptoms and the occurrence of death, or the time when the patients were subjected to operation.

Paschen¹ has reported the results obtained by operation in 268 cases which he collected from various sources, and while his figures do not offer a very hopeful outlook for patients affected with these growths, nevertheless they show that operation is always worth resorting to except when some associated condition absolutely contra-indicates it. Only 17.7 per cent. of the patients were free from recurrence at the end of three years, although in Paschen's own series of cases, 54 in number, 35.19 per cent. have passed the three year limit. Inasmuch as experience seems to prove that recurrence is rare after three years, these latter figures show a very good result, using the expression in a relative sense, of course, as applied to any malignant condition. There were 28.7 per cent. who died of local recurrence or metastasis, and 8.58 per cent. who succumbed to intercurrent disease, the fate of 8.21 per cent. being unknown.

A CASE OF PRIMARY ADENOCARCINOMA OF THE KIDNEY has been reported by J. S. Eisenstaedt.² The neoplasm consisted of a nodule 4 cm. in diameter situated on the convex border of the organ about midway between the two poles. There seemed to be a gradual passing of normal kidney tissue into neoplastic tissue. The tumor thus presented, in parts, a massive arrangement of densely packed cells, and in other places a papillary structure showing hyperplastic and chronic retrograde changes. There was very little supporting stroma between the cells of the growth, the whole picture suggesting the belief that the tumor

¹ Archiv f. klin. Chirurgie, October, 1915, vol. cvii, No. 2.

² Urological and Cutaneous Review, February, 1916.

originated from the glomeruli rather than from the uriniferous tubules. This case is of interest clinically because of the fact that it was ushered in by an attack of hematuria which was painless, and which persisted for two years, after which time it became painful, the pain being probably due to a small stone in one of the calices. The patient seemed well seven months after operation.

Inflammatory Stricture of the Ureter. At the last meeting of the American Urological Association, Guy L. Hummer,¹ of Baltimore, made a detailed report upon simple inflammatory stricture of the ureter, which he showed to be more common than it is usually believed to be, as his cases up to November, 1915, totaled 50.

The most potent etiological factor is thought to be inflammation of the ureter produced by infection from some distant suppurating focus, which, for instance, may be situated in the intestines, or the tonsils, or the teeth. In some cases there may be simultaneous involvement of the kidney, so that a pyelonephritis, as well as a ureteritis, is produced. He also recognizes the possibility of inflammation taking place from the passage of infected urine through the ureter and from ascending vesical infection, although the latter is considered extremely rare. In such cases he considers infection through the lymph channels the most common mode.

The symptoms are usually those of obstruction, and consist of dull heavy pain in the lumbar region which sometimes undergoes acute exacerbations. This pain may be transmitted along the course of the ureter, and there may also be vesical, and even rectal, tenesmus. If infection be present, there may be, in addition to these symptoms, those due to the absorption of pus, such as chills, elevation of temperature, sweats and considerable prostration. Exacerbations are particularly likely to occur after exposure to cold, dampness and wet, and in some such instances the author has observed localized pain at the site of the constriction in the ureter.

Diagnosis is made from the history of the symptoms as above outlined, from careful microscopic examination of the urine, and by physical methods, particularly ureteral catheterization. Attention is called to the fact that the urinary findings may be negative. As a rule, however, a few red blood cells, together with some leukocytes, are present. After attacks of colic the urine will be more likely to contain an abundance of blood and pus than during periods of quiescence. In women, if the stricture is situated low down near the bladder wall, it may be possible to detect it by palpation through the vagina. Naturally, repeated obstruction to the ureteral catheter at the same site, with the absence of any evidence of stone following x-ray examination and the use of the wax-tipped catheter are the circumstances which point most strongly to the presence of a stricture. If there be an associated hydronephrosis,

¹ Transactions of American Urological Association, 1915.

further evidence of stricture is furnished. Dilatation through the cystoscope is the treatment recommended. In cases in which infection is present, lavage of the renal pelvis is also practised. When the kidney has been destroyed, its removal is considered the most conservative measure. The author had 6 cases in which this was necessary. In the cases in which dilatation cannot be practised through the bladder, dilatation from above downward, through an opening made above the stricture, is advised. This method was resorted to in 8 cases, in 6 of which the results were excellent. The ureter was exposed by an extraperitoneal incision, incised and dilated.

Foreign Bodies in the Bladder. A paper on this subject, based upon a series of cases occurring in the Mayo Clinic, has been published by Edward S. Judd.¹ In this series of cases, as is usual, the most common route of entry was through the urethra, although a few cases which are unique as regards the route of entry were recorded. With reference to the substances which were passed into the bladder through the urethra, the author mentions 3 cases in which hairpins were the offending articles, and 1 case in which a piece of chewing gum had been introduced. More interesting are the cases in which the route of entry was obscure. An example of the cases in which foreign bodies may find their way into this viscus, without leaving any lesion in the wall at the site through which they passed, was that of a boy who, twelve years previous to the time he came under observation in the Clinic, was wounded with a knife, the blade of which broke off in the tissues and could not be found. Twenty-one months before examination at the Clinic, the patient noticed an increased frequency of urination and passed some blood. Later, some interruption of the stream developed, together with pain in the left hip, which radiated to the back and produced some nausea. He became much reduced in general health, began to cough, and had night-sweats. Cystoscopic and x-ray examination revealed the presence of a foreign body, and, at operation, a knife blade was found in the interior of a calculus. No lesion of the bladder wall could be detected.

Another interesting case was that of a patient who had passed fragments of bone through the urethra, and in whose bladder operation revealed the presence of pieces of bone which evidently had worked their way into the viscus from an old tuberculous osteomyelitis of the left femur. In this case, likewise, there was no apparent lesion of the bladder wall.

Legueu² describes a method of extracting bullets from the bladder by means of a lithotrite which he has modified slightly by hollowing out the tips of the blades so that they will more satisfactorily hold the smaller end of the bullet. The instrument is passed in the usual way, but after its beak has reached the bladder its distal end is raised so as to

¹ Papers of Mayo Clinic, 1915, vol. vii.

² Journal d'Urologie, October, 1915.

depress the vesical floor and thus cause the bullet to slip down into the hollow produced by this manipulation. If the bullet be seized in its transverse axis it will slip out of the jaws of the lithotrite, but if grasped by either end it can be easily extracted merely by withdrawing the instrument from the bladder. The author states that the correct position of the bullet in the extracting instrument can be ascertained by rectal touch. He considers cystoscopic examination the only certain method of determining the presence of a bullet in the bladder; for, although radiography will show the shadow of a bullet in the pelvic cavity, it does not necessarily prove that it is within the bladder itself. If two exposures be made, however, with the patient in different positions, and the shadow is seen to change place, then it is safe to assume that the bullet is in the bladder. Examination with the sound is not considered at all trustworthy.

In this respect, the case of an officer who was wounded at the battle of the Marne is interesting. He had been transferred from hospital to hospital, for it was thought, as the result of *x*-ray examination, that the bullet was embedded in the cellular tissue of the pelvis, and it was desired to give the patient the most expert surgical attention. When he finally reached Paris, where he intended to have an operation, cystoscopic examination showed the presence of the bullet in the bladder. In a few days he went back to his command. Another interesting case was that of a soldier who returned to the front the day after a bullet was extracted from his bladder.

Legueu states that he has seen a considerable number of injuries to the bladder among soldiers. He has removed, by suprapubic cystotomy, fragments of shells some of which had been in the bladder so long that they had become encrusted with the salts of the urine. In many cases these foreign bodies gained access to the bladder through wounds inflicted a considerable distance away from that viscus. In one case the author removed a piece of shell that had entered the body through the left shoulder and traversed both the thoracic and abdominal cavities.

G. Grey Turner¹ has also reported upon foreign bodies in the bladder resulting from gunshot wounds, and considers that oftentimes the history of the case is not sufficient to enable one to make a correct diagnosis. He, too, advises that *x*-ray pictures should be taken with the patient in various positions and with the bladder both empty and full. Radiography, however, is not considered sufficient in all cases, inasmuch as certain substances that do not give a shadow may be carried into the bladder through wounds, even in remote parts of the body; for that reason a routine cystoscopic examination is always advised. An interesting case seen by the author was that of a man who was wounded in the sacral region by a bursting shell, with injury to the rectum which

¹ London Lancet, May 6, 1916.

eventually caused a large fecal fistula. The patient finally began to complain of difficulty in urination, and, upon cystoscopic examination, evidences of inflammation at the base of the bladder, most pronounced at the upper limit of the trigonum, were found. Opposite this area a hard mass could be palpated through the rectum. It seemed to be situated in the bladder wall. X-ray examination showed it to be a piece of metal. It was not deemed advisable at the time to remove it surgically because of the danger of producing a rectovesical fistula. The author believed that it would gradually ulcerate its way into the bladder and eventually be passed through the urethra. Another interesting case was one in which a piece of shell casing, after causing considerable trouble, was passed spontaneously through the urethra. This foreign body gained access to the bladder through a wound of the buttock caused by an exploding shell.

Mesothorium and Diathermy in the Treatment of Malignant Vesical Tumors. An exceedingly interesting report on the use of mesothorium in conjunction with diathermic treatment was made by G. Kolischer¹ at a meeting of the Chicago Urological Society last autumn. He reported 4 cases of inoperable carcinoma in which surprising improvement in the local condition, together with marked relief of symptoms, was brought about by this treatment.

The first case was one in which the lower half of the bladder was occupied by a large cancer, which, under the use of mesothorium, underwent such marked retrogression that at the end of four months a cystoscopic examination revealed only a small nodule situated near the left ureter. This nodule was fulgurated and after a few days another cystoscopic examination was made, which showed that it had disappeared. A second case was one of cancer of the trigonum. After seven months' treatment with mesothorium, cystoscopic examination showed that the neoplasm had been reduced to the size of a pigeon's egg. The third case was also one in which the trigonum was involved, the neoplasm having developed after a prostatectomy. Two months before the patient came under observation he began to be troubled by dysuria and passed some blood with the urine. It was impossible to get any instrument through the posterior urethra, therefore a suprapubic cystotomy was performed, and an extensive cancer involving the trigonum was found. After two months of mesothorium treatment, the tumor had disappeared, and a No. 27 French sound could be easily passed through the urethra. The fourth case was also one of carcinoma of the trigonum, producing distressing symptoms. Under mesothorium the patient improved so much, both locally and generally, that he declined further treatment, and even refused to have another cystoscopic examination made.

With reference to technic, the author states that when the meso-

¹ Transactions of the Chicago Urological Society, 1916.

thorium is applied through the urethra it is enclosed in a gold filler, but when used through a suprapubic opening into the bladder it is placed in a silver or brass container. When possible, the urethral method of application is preferable, but in cases in which it becomes necessary to open the bladder for the relief of urgent symptoms or for the making of a diagnosis in cases in which instruments cannot be passed through the urethra, the applications are made through the suprapubic wound. It is in this latter class of cases that diathermy is resorted to as an auxiliary measure, and Kolischer considers it a very valuable adjunct to the other treatment. It controls hemorrhage and destroys infectious material, in addition to reducing the neoplasm in size and changing its consistency, thereby rendering its deeper parts more accessible to the rays. In order to give the patient all the benefit of the appliances in his department, the author also employs filtered *x*-rays passed through the abdominal wall while the mesothorium is still inside the bladder, or in some cases shortly after its removal. He states that he does not consider the rays curative in any sense of the word, although they exert what he terms a certain cleaning-up action, by which is meant that the cystitis seems to improve under their use, hemorrhage becomes less, and pain is controlled to a certain extent. He emphasizes the circumstance that in no case has he observed a tumor which had been treated solely by the *x*-rays. Furthermore, he expresses the opinion that the rays are of double value in preventing recurrence after resection of the bladder for malignant tumor.

The results obtained with mesothorium, as reported by Kolischer, are truly surprising, and, if further experience with it shall demonstrate its uniformity of action, certainly much will have been gained in the treatment of a trying and unsatisfactory class of cases.

In discussing Kolischer's paper, Lower, of Cleveland, remarked that he had obtained excellent results, so far as relieving the patients is concerned, by burning the tumor down with the actual cautery, and mentioned some cases in which the wound in the bladder had closed after this procedure, and the patients had been able to void urine spontaneously and to completely empty the bladder, and had also been free from hemorrhage. I can confirm Dr. Lower's experience, although I have probably not utilized the method in nearly as many cases as he has. For this purpose I have used the ordinary Paquelin cautery after excising as much of the growth as could safely be removed. In every case in which the method has been employed there was benefit. The effect has been comparable to that obtained by the same method in the treatment of inoperable uterine carcinoma.

The Treatment of Chronic Trigonitis. The treatment of this troublesome condition has been thoroughly discussed by H. W. E. Walther¹

¹ *Medical Record*, 1916, p. 853.

who accords preference to instillations and topical applications of silver nitrate. The instillations are used twice weekly and vary in strength from 0.25 per cent. to 2 per cent., the bladder being anesthetized with novocaine or other local anesthetic. Stronger solutions of silver can be applied through the Kelly cystoscope in cases in which the trouble does not yield to instillations, and for this purpose the author recommends at first a 5 per cent. solution, which may be increased if desired. It is found that some cases require the application of pure stick silver, although the latter should be used with caution. Curettement of hypertrophied papillæ is recommended, together with puncture of any cysts that may be present, both procedures being carried out through the Kelly cystoscope in the female and through any of the operative cystoscopes in the male. Curettage through a suprapubic opening is reserved for those intractable cases which resist all other methods of treatment, and should be combined with the use of such other measures as fulguration or the actual cautery point if lesions are found which seem more amenable to this latter procedure. Such an operation is followed by drainage through the wound. The author's experience with irrigations in this disease has not been at all satisfactory.

THE PROSTATE.

Prostatectomy. Local anesthesia for prostatectomy continues to receive attention, and during the last year two noteworthy contributions have come to my attention. One by Hertzler,¹ of Kansas City, discusses the combined method of sacral blocking and periprostatic infiltration. Sacral anesthesia alone is stated to fail in about 10 per cent. of the cases, even in the hands of experts, and, consequently is not considered at all satisfactory for general use. For introduction into the sacral canal, the author uses 60 c.c. of 0.5 per cent. novocaine solution containing 10 minims of epinephrin, with from 60 to 90 c.c. of a 0.6 per cent. solution of quinine and urea hydrochloride. He states that the danger of introducing the needle into the spinal dura is much exaggerated, and that it would be difficult deliberately to puncture the canal with a straight needle. In hundreds of injections which he has made, the dura has never been punctured.

Two important factors contributory to successful anesthetization of the sacral nerves are the use of a sufficient volume of fluid and passing the needle sufficiently high into the sacral canal. The only ill effect this author has ever known to follow sacral anesthesia is a transitory anesthetization of the sciatic nerves, and for an operation like prostatectomy he does not consider this sequel at all important, as it will have passed away before the patient gets up and about.

¹ Journal of American Medical Association, April 29, 1916.

After the use of quinine and urea, some patients have complained of numbness. The prostate is infiltrated through a suprapubic incision, novocaine and epinephrin solution being employed. The periphery of the gland and the deep portion of the prostatic urethra are injected. Enucleation is begun after the lapse of ten or fifteen minutes. The author has devised a prostatic retractor shown in Fig. 28, which gives very satisfactory exposure of the bladder and prostate.



FIG. 28.—Prostatic retractor, used with both perineal and suprapubic prostatectomy.

Charles Perrier,¹ of Geneva, also discusses the subject, and after reviewing the various methods which have been used, describes a combination method which has given him great satisfaction in 5 cases. The first step consists in anesthetizing the suprapubic portion of the abdominal wall by infiltrating it with a 1 to 200 novocaine-adrenaline solution, the quantity varying according to the thickness of the tissues, after which the superficial tissues in front of the anus as far as the tuberosity of the ischium on either side are infiltrated with the same solution. This second step renders the deep injection of this region painless. The third step consists in infiltrating the prostate beneath its capsule. Special needles from 12 to 15 cm. in length are used for this purpose. The left index finger introduced into the rectum serves as a guide. For the fourth step the sacral canal is injected with a solution of the strength of 1 to 100.

The author states that the operations he has done under this combina-

¹ Journal d'Urologie, October, 1915.

tion method have been entirely painless, and that he has not seen any evil result from it. He considers that it will prove equally as satisfactory in the cases of very fat patients and in those who have hard fibrous prostates that are difficult to enucleate as it will in thin patients and those in whom enucleation presents no special difficulties. He has not noted any sloughing of the wound.

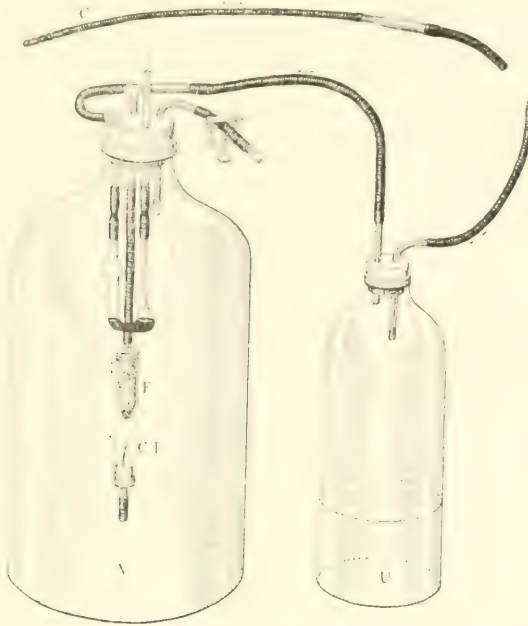


FIG. 29.—Diagram showing relations of various tubes. Arrows indicate direction of air flow.

In discussing local anesthesia for prostatectomy in this review some two or three years ago, the opinion was expressed that there are very few patients who cannot take ether when properly given by the drop method. In the interim this opinion has not undergone any modification, and, while recognizing the advantages that any satisfactory method of local anesthesia may possess in certain exceptional cases, I have not resorted to it. It would seem that in certain cases the gas and oxygen method has much to commend it.

An ingenious *vacuum apparatus* for securing drainage after prostatectomy has been devised by E. G. Davis,¹ of Baltimore. It consists essentially of a larger and a smaller bottle, the former being exhausted of air and then gradually filled again from the smaller one as the urine is drained from the bladder by suction. The capacity of the larger bottle is 8 liters, that of the smaller, 2 liters. The larger is provided with

¹ Journal of the American Medical Association, May 27, 1916.

a rubber stopper having four perforations for the accommodation of two L-shaped glass tubes, one T-shaped glass tube, and a straight tube. The smaller bottle is provided with a rubber stopper having two holes bored through it, through which straight glass tubes are passed. A catheter perforated in several places at the tip leads from the bladder to a rubber tube 5 mm. in diameter which connects it with the smaller bottle. The capillary tube is held in place in the larger bottle by a constricted outer tube of glass, the part above the constriction being filled with cotton for the filtration of the incoming air. The rate of air flow through the capillary tube is determined and regulated by connect-



FIG. 30.—Detail of capillary tube, with outer protecting glass sheath. *F*, cotton filter; *CT*, capillary tube.

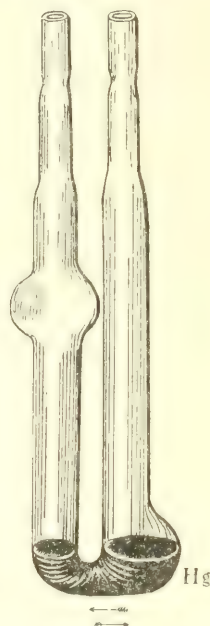


FIG. 31.—Detail of mercury manometer. Air may pass through in either direction, as indicated by the arrows. *Hg*, mercury.

ing the lower and large end with a vacuum of known strength and causing the air which enters through the tube to bubble through a column of water as it is drawn into the vacuum. The most satisfactory caliber of capillary tube is that which permits an air-flow of 70 to 80 bubbles into a vacuum that will sustain a column of mercury 60 cm. in height. The manometer consists of a small quantity of mercury in the pump of a U-shaped tube, one limb of which communicates with the smaller bottle after the T-shaped tube connecting with the capillary tube has been given off; the other limb perforates the rubber stopper to lead into the air. At the angle of the U in this latter tube, a bulb has been

blown, and there is a smaller bulb on the other arm 5 to 6 mm. from the bottom. The former bulb acts as a reservoir for the mercury and allows the passage of air into the exterior. When the air in the smaller bottle becomes condensed—that is, when urine collects in the bottle faster than air is expelled through the capillary tube—the second bulb acts as a similar reservoir when the air in the smaller bottle becomes rarified—that

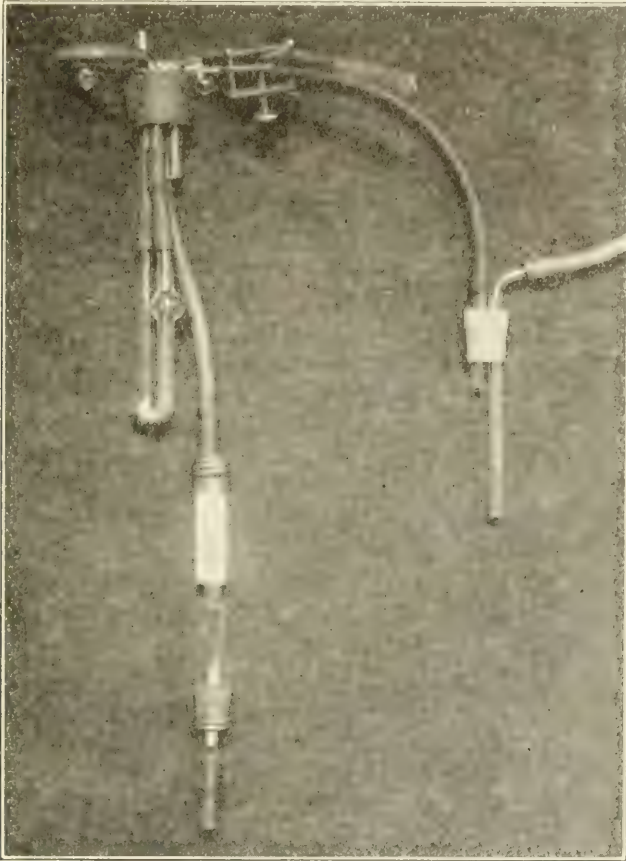


FIG. 32.—Capillary tube, manometer, rubber stoppers, and connecting tubing, shown without bottles.

is, when the air escapes faster than the urine collects. The urine bottle must be empty when it begins to fill, and the air must be exhausted from the vacuum bottle at intervals of not less than forty-eight hours. By this means the bladder wound is kept perfectly dry and clear.

Another *apparatus for securing drainage of the bladder* has been described by Joseph Hume and Samuel Logan,¹ of New Orleans. It

¹ New Orleans Surgical Journal, July, 1916.

consists essentially of a suction pump regulated by clock-work, and run by electricity. It can be set to work for a certain time and can be started or stopped by the patient himself. When this apparatus is used, the dressings need be changed only once in seventy-two hours, so that the wound is kept dry and in good condition, with the result that complete healing has taken place in from two to three weeks. The size of the drainage tubes is gradually reduced. The first one consists of a modified Freyer tube containing within its lumen an inner suction tube. This apparatus is left in from forty-eight to seventy-two hours, after which it is replaced by a smaller tube, which in turn is left in from two to four days. When it is removed, an ordinary retention catheter or a smaller sized suction tube will suffice. The authors still use gauze packing in the cavity made by the removal of the prostate, leaving it in for from forty-eight to seventy-two hours.

The Treatment of Neuralgia in Vesical and Prostatic Disease. The relief of sacral neuralgia produced by neoplasms of the prostate and bladder merits special consideration, and any measure which will completely overcome it seems worthy of trial. An article by Louis A. Sur-raco,¹ of Montevideo, in which he reports the successful treatment of 4 cases, has recently been published. He has used injections of alcohol in the posterior sacral foramina, usually the 2d, 3d and 4th, and in every case has secured relief of long duration. His method for finding the aperture is as follows: The second aperture is on a horizontal line situated about 2 cm., or a finger's breadth, below the posterior superior iliac spine; the third is 2 cm. lower, and the fourth one likewise 2 cm. below the third. If a vertical line be drawn on either side 2 cm. away from the spinous processes, the points at which it intersects the three horizontal lines previously constructed will represent the position of the various foramina. The second foramen is much deeper than the others, particularly the fourth, which is very superficial. Once the needle has been introduced into a foramen 2 c.c. of alcohol is injected into it. Of course, it will be understood that the injection must be made upon both sides. As the immediate effect of the alcohol is extremely painful the patient is given one or two preliminary injections of scopolamine and morphine. After a somnolent condition is produced, no pain is experienced. In 3 of 4 cases in which this treatment was resorted to, only one injection was required. In the fourth case, however, a second injection had to be given. One patient remained free from pain for five months and two of the others for three months. It seems to me that this method is well worth trying in those hopeless cases in which the last weeks or months of life are continuous torture.

Syphilis of the Prostate. Very little has been written upon the involvement of the prostate and bladder in syphilis. Therefore, any contribu-

¹ Journal d'Urologie, October, 1915.

tion to the subject is of interest. A recent paper by Ravogli,¹ of Cincinnati, has come to my attention during the year. He considers the manifestations of the disease in the prostate itself as well as the prostatic urethra, and in both its early and late stages. In the secondary stage, the prostatic urethra may be the site of superficial ulcerations corresponding to the ordinary mucous patch, or more likely to those of the condylomatous or papular type. In such cases the passage of an instrument, even though done with the utmost gentleness, is painful and causes some hemorrhage by excoriating the ulcerative lesions. The author has had a number of cases of this kind. One which he reports as an example was that of a young man who had had several attacks of gonorrhea of which, however, he had been apparently cured. Two years previous to the time he came under observation he contracted syphilis. He consulted the author with the hope of being relieved of dysuria and frequency of micturition. His urine was turbid. Examination with the sound imparted the sensation of some induration in the bulbar region. Rectal examination showed that the prostate was slightly enlarged and had a few irregular nodules on its surface. After the examination, a deep irrigation was given, but no relief was obtained; in fact, the symptoms became more acute. After their subsidence, a urethroscopic examination was made, and two ulcerations were found in the prostatic portion of the canal. These were touched with a 3 per cent. solution of silver nitrate. Active anti-syphilitic treatment was instituted, and, after a short time, the patient's symptoms improved, and a subsequent urethroscopic examination showed that the ulcerations had healed.

An interesting case of late syphilis in which the prostate was involved was also reported. A gumma within the substance of the gland had partly occluded the deep urethra. Prostatotomy was performed and a considerable quantity of grumous fluid and gland detritus was evacuated. The patient made an excellent recovery. Other similar cases, though milder in degree, did well under antisiphilitic treatment, especially salvarsan.

Primary Tuberculosis of the Prostate Gland. Primary tuberculosis of the prostate gland is very rare and for this reason a case recently reported by Irvin S. Koll,² of Chicago, is thought worthy of mention in this review. The case was that of a man, aged sixty-one years, who entered the hospital suffering with complete retention of urine, which was supposed to be dependent upon hypertrophy of the prostate, as an examination of the gland through the rectum revealed the fact that it was very much enlarged. Cystoscopic examination showed that the median lobe projected into the bladder. A preliminary cystotomy was done under local

¹ Urological and Cutaneous Review, March, 1916.

² Annals of Surgery, October, 1915.

anesthesia and ten days later the prostate was removed. A persistent fistula made it necessary for the patient to remain in the hospital five months, and caused him to return later for a secondary operation for closure of the same, which fortunately proved successful. Microscopic examination of paraffine sections of the gland showed areas of typical tuberculosis with some caseation and glandular hyperplasia. Tubercle bacilli were found in some of the caseated areas. As soon as the diagnosis of tuberculosis had been established, tuberculin was begun, and, inasmuch as there was not the slightest reaction even to very small doses, it would seem that the author's belief that he was dealing with a primary lesion in the prostate was well supported.

In investigating this subject, the author was able to find only 2 probable cases of primary tuberculosis of the prostate, but he does not believe that this paucity of reported cases proves that primary invasion of the gland is so exceedingly rare, rather holding to the idea that a greater number of cases would have been recorded if more frequent microscopic examinations of enucleated prostates were made.

Cysts of the Prostate. A complete exposition of this subject together with a report of a case has been made by John H. Cunningham,¹ of Boston. The author has collected the reports of cysts of the prostate from the literature. Of dermoid cysts he could find but one case, that described by Quervain, and a doubtful case. Other varieties are either dependent upon obstruction of the prostatic ducts, with dilatation of the acini from retained secretions, or are due to dilatation of the vesicula prostatica, or are echinococcus cysts.

The cysts due to obstruction of the prostatic ducts are usually small, single and unilocular, and are perhaps formed by the coalescence of several dilated acini. They may project into the prostatic urethra, or, less commonly, into the bladder near the sphincter. The cysts contain an albuminous fluid showing epithelial cells, leukocytes and detritus, but no microorganisms. These cysts are supposed by Englisch to be congenital, but this view has been disputed. Englisch found five instances of cyst formation near the sinus pocularis in autopsies on 70 male children. Cunningham, in a resumé of the literature, gives a summary of 15 recorded cases, in most of which the diagnosis was made postmortem. In 1 case the cyst attained the size of an egg.

The class of cysts due to dilatation of the vesicula prostatica are also supposed to be congenital, and caused by a defect in the process of obliteration of Müller's duct. Springer found 2 cases in autopsies on 62 male infants who died soon after birth. They are unilocular, may be small or large, and may interfere with urination or ejaculation. The swelling may project into the rectum as a rounded tumor resembling bilateral lobe enlargement of the prostate gland. A distended sinus pocularis

¹Surgery, Gynecology and Obstetrics, November, 1915.

without true cyst formation is, in the author's opinion, an acquired condition, which may be diagnosed by the inflammatory character of the prostatic secretion expressed *per rectum*. It may possibly, however, lead to the formation of true cysts. The author has collected 5 cases of cysts of the vesicula prostatica from the literature (4 of which were post-mortem cases) and adds a case of his own, which will be mentioned below.

Echinococcus cysts of the prostate are usually secondary to echinococcus cysts elsewhere in the body. A full list of the authors dealing with this class of cysts is given.

Diagnosis of the first class of cysts is practically made solely by urethroscopy or cystoscopy.

The author believes that a valuable sign in cysts of the second class is the increased space found between the urethra and the rectum in instances where the usual sign of a carcinomatous prostate is absent. The increased tissue is detected with an instrument in the urethra and one finger in the rectum. A sense of fluctuation may be present.

Echinococcus cysts are still more apt to fluctuate, may also give the sense of increased tissue between the urethra and the rectum, and are more apt to be seen projecting into the bladder. Then, again, these cysts are apt to appear elsewhere in the body.

With regard to *treatment*, the method employed must depend on the type of cyst and on the special features of the cyst in a given case. The first class have been removed by suprapubic operation, but if a cyst of this type involving the prostatic urethra should be recognized clinically, and if they can be seen by a deep urethroscope, there is no reason why they should not be removed by the use of the new instruments for operating in the deep urethra. A small cyst of the sinus pocularis has been destroyed through a deep endoscope. In large cysts, an attempt should be made to remove the sac with, or without, the prostate by the perineal or suprapubic route, preferably, however, by a dissecting perineal operation. An echinococcus cyst should be removed, or should be incised and drained, through the abdomen, perineum or rectum.

The author's case showed *postmortem* a cyst of the vesicula prostatica the size of a lemon. The patient was fifty-eight years of age, and had been suffering for a year with greatly increased frequency of urination. Rectal examination showed all the signs of an enlarged but not tender prostate, from which a fluid could be expressed into the urethra. Palpation *per rectum* with the cystoscope in the urethra showed an increase in the amount of tissue posterior to the urethra. There were 25 ounces of residual urine.

Operation was done through a median incision and part of the prostate removed. The cyst was ruptured and drained. The patient died four days later. Autopsy showed a cyst of the vesicula prostatica and a carcinomatous prostate, with secondary nodules in the mesentery and pelvis.

Rhabdomyomatous Sarcoma. A case of this exceedingly rare neoplasm of the prostate has been reported by J. B. Squier,¹ of New York. It occurred in a man, forty years of age, whose general condition seemed good at the time he came under observation. He gave a history of having had for three months a painless terminal hematuria, which, however, was not constant, although at some time during the day the blood would appear after micturition. He also complained of some frequency of urination. Examination of the prostate through the rectum showed it to be symmetrically enlarged and of unusually hard consistency. No evidence of periprostatic involvement could be found. The cystoscope showed considerable trabeculation of the bladder, but there was no projection of the prostate into that viscus. Diagnosis of prostatic tumor was made and radical removal of the gland, together with the neck of the bladder and the seminal vesicles, was performed through a perineal incision, after which an anastomosis was made between the urethra and the divided neck of the bladder, and a gauze drain introduced. Recovery from the operation was uneventful, and, after the patient left the hospital, a course of x-ray treatment was begun with the hope that it might prevent recurrence. Two months after operation, however, a recurrence took place in the scar, and the new growth rapidly extended to the rectum. At the time the case was reported, the patient's condition was considered hopeless. With regard to the structure of the tumor, the gross tissues showed two irregular fragments, a portion of each being plainly encapsulated. In some areas, dilated tubules containing yellowish material could be distinguished in the smooth, white stroma which constituted the tumor. Upon microscopic examination, three distinct types of structure were found: A glandular type showing evidence of inflammation, a dense fibrous type intermingled with gland tissue and showing muscle fibers in certain areas, and areas of pure spindle-celled sarcoma. There were also scattered cells of this kind in the second type of tissue. Microscopic diagnosis in this case was glandular hyperplasia of the prostate with the formation of a rhabdomyomatous sarcoma. The rarity of this type of tumor makes the case worthy of notice in this review. Squier mentions 3 other cases collected by Kauffmann. I remember another case reported some years ago by Mr. Greig, an English surgeon.

Metastatic Prostatitis. Inflammation of the prostate is usually associated with the thought of gonorrhea or instrumental injury, the latter being particularly likely to cause suppurative inflammation in the subjects of prostatic hypertrophy who are likewise suffering with vesical or urethral infection. The occurrence of prostatitis as a complication of such constitutional conditions as pyemia, smallpox, typhoid fever, or purulent collections in remote parts of the body, however, is well estab-

¹ Surgery, Gynecology and Obstetrics, September, 1916.

lished, although such cases are not often met with. In a recent contribution to this subject Wildbolz,¹ of Berne, reports 14 cases of acute prostatitis which developed as a sequel to influenza, and 22 others in which tonsillitis and intestinal trouble were the most common preceding ailments. In only 5 cases did abscess formation take place. The specific bacillus of influenza was not recovered from the prostatic secretion, only the more common pathogenic organisms being found. This is quite in accord with the rarity with which the gonococcus is recovered from prostatic abscesses. One patient developed prostatitis while affected with a large boil on the neck, and later a perinephric abscess formed, staphylococci being recovered from all three of the lesions. Another patient's trouble followed a crop of sties.

The symptoms and treatment are not different from those of more frequent forms of prostatic inflammation, the former consisting of bearing down in the perineum and rectum, frequent, difficult micturition, and in some cases hematuria, together with the constitutional disturbances which usually accompany such local manifestations. It seems, however, that urinary symptoms may be absent, for one patient who had a prostatic abscess which had been opened and drained was free from any disturbance of micturition. A urine free from pus, with the objective symptom of prostatic involvement, points at once to the metastatic origin of the trouble. One patient developed epididymitis. This complication I have seen follow a case of prostatitis presumably due to colon bacillus infection.

The author considers that the prognosis is favorable and recommends treatment along the usual lines, with prompt evacuation of the pus by perineal incision as soon as its presence can be determined.

THE SEMINAL VESICLES, TESTICLES, AND CORD.

Seminal Vesicle Infections. In discussing the surgical treatment of seminal vesicle infections in this review three years ago, the opinion was expressed that the operations of vesiculotomy and vesiculectomy were procedures to which more attention should be given. That such a view has been shared by other surgeons is evidenced by occasional contributions to the subject which have been made since that time. The literature, however, is by no means voluminous, a circumstance which is probably due to a laudable conservatism on the part of a majority of surgeons, who feel that all other therapeutic measures should be resorted to in the average case of vesiculitis before operation is considered.

Studies in the normal and morbid anatomy of the vesicles, as well as more careful investigation of the clinical phenomena resulting from their

¹ Correspondenz-Blatt f. Schweizer Aerzte, February 5, 1916.

involvement in diseased processes, taken in conjunction with results already obtained by operation, has led to a better understanding of the importance of these small and remotely situated organs, the difficulties to which they give rise, and the relief which may be expected from judicious surgical treatment. That more definite knowledge may be obtained as time goes by seems to be the belief of all those who have devoted themselves to the investigation of the subject, as they recognize that at present the indications for surgical attack upon the vesicles are not altogether certain.

Since Fuller's paper was reviewed in 1913, notable contributions to the subject have been made by J. Bentley Squier and Hugh Cabot, and also reports on *x*-ray studies by Belfield and Thomas, both of which received notice in this review. Luy's paper, in which emphasis was placed upon the necessity of treating the associated deep urethral lesions, and particularly of securing patency of the seminal ducts, likewise received adequate notice.

During the past year, three important contributions to the subject have come to my attention. One by Louis E. Schmidt,¹ of Chicago, is clearly characterized by the rational views therein set forth in it. He takes the stand that every case should be studied upon its own merits and that a decision to operate should not be reached hastily; furthermore, he advises that the older measures, followed eventually by vasotomy, should be thoroughly tried before the more serious operations are considered. Circumstances which must be taken into consideration are the virulence of the infection, the duration of the disease, the local and systemic disturbances which have been produced by it, and the degree of improvement which follows other measures. Even though improvement be slow, provided it is perceptible, there is ground for hope that a continuation of conservative treatment may eventually bring about a cure. Particularly in cases in which nervous disturbances and marked hypochondriasis are evident should one hesitate before deciding upon radical operation.

In my previous discussion of the subject, this view was taken with regard to the nervous class of cases. With regard to a choice between vesiculotomy and vesiculectomy, the former is advised in acute cases, in which free pus and severe constitutional symptoms are present. Immediate relief of pain and conservation of the structures involved have invariably followed such a procedure in Dr. Schmidt's practice. If it be found, at the time of operation, that the vesicle wall is thoroughly riddled with miliary abscesses, then vesiculectomy is considered the preferable operation. So likewise is it preferred in cases in which there is marked infiltration of the vesicles with perivesiculitis which renders them adherent to surrounding parts. Among distinctive conditions

¹ Journal of the American Medical Association, January 15, 1916.

calling for radical operation are attacks of colicky pain simulating ureteral or appendicular colic. In such cases Dr. Schmidt has usually found calculi present, although the symptoms can well be accounted for by the anatomical relation of the vesicles, notably the position they hold to the ureter.

Another noteworthy contribution has been made by Edward W. White,¹ of Chicago, who reports the results obtained in a number of cases, discusses the indications for operation, and gives a very complete exposition of the symptomatology. He practically agrees with Schmidt as to the indications for operation and the choice between vesiculotomy and vesiculectomy. Six operative cases are reported. The majority have been treated within the past year, so that final results cannot yet be determined. The immediate results, however, seem very favorable. The relief of pain, the evacuation of pus, and the removal of hard fibrous vesicles which produced great discomfort were, in the order named, the conditions for which operation was resorted to in this series of cases.

As to symptomatology, both Schmidt and White consider that Belfield's classification which referred the disturbances to the genital organs, urinary organs, rectum, abdomen, and then made a fifth grouping under general systemic disturbances, will cover all cases. White states that in 90 per cent. of the patients who have come under his observation nervous symptoms were present. This he attributes largely to the effect of long-continued pain. With reference to the urinary symptoms, he describes an interesting condition revealed by the cystoscope, namely: a hyperemia and edema of that portion of the bladder in relation to the seminal vesicle. Great importance is attached by both authors to the presence of blood in the vesicular contents, and they both agree that its persistence, either in the secretion obtained by massage or in the ejaculate, should lead one to consider the advisability of a radical operation. The rectal symptoms are those so well known as being associated with disease of the prostate and vesicles, consisting of a sense of weight or obstruction in the lower bowel, with burning pain and general irritability of the mucosa. Naturally, the abdominal symptoms depend upon the irritation of the peritoneum and the close relation of the vesicle to the bladder and ureter, and even the appendix. Thus suprapubic pain, as well as attacks of colic, are not uncommonly met with.

With reference to systemic conditions, involvement of the joints naturally will be the one most frequently met with, except the high temperature and general constitutional disturbance associated with acute cases. Some of the most gratifying results obtained by different surgeons, notably by Fuller and Squier, related to joint involvement.

¹ Urologic and Cutaneous Review, July, 1916.

A symposium on this subject was held before the Chicago Urological Society. If I remember rightly, it was there that Dr. White's paper was read. E. O. Smith,¹ of Cincinnati, in reporting at this meeting the results of his investigations into the anatomy and pathology of the seminal vesicles, called attention to the necessity of making multiple incisions in order to establish satisfactory drainage. He showed that the tubules are so arranged that a single incision in the lower part of the vesicle will not suffice. In a considerable number of specimens which he examined, at least one half showed evidence of disease, a circumstance which the author attributes to the difficulty of the vesicle draining itself in a satisfactory manner. These findings have led him to discountenance long-continued massage in refractory cases. No calculi were found in the specimens examined, and the author quotes Fuller to the effect that, in more than 700 vesiculotomies, calculi were found in only 7 cases and only once in both vesicles in the same patient. It would seem, from these findings, that the cases of colic of the renal type are due to adhesions between the vesicle and ureter.

That vasotomy followed by injections of argyrol has proved highly successful in the practice of some surgeons was well exemplified in the discussion which followed the symposium at Chicago. Wm. E. Jost,² particularly, spoke in high praise of Belfield's work in this connection, which he characterized as a decided victory for the genito-urinary surgeon and the patient alike. He considers it the only recognized method of eradicating infection in the seminal tract, and while such an opinion might perhaps be considered unduly enthusiastic by many, it nevertheless shows the difference in results obtained by the speaker before and after his use of the method. In 40 cases in which Jost has employed vasotomy, other forms of treatment, such as massage, injections, instillations, and the use of vaccines, had been tried for considerable periods of time, varying from a number of months to several years, and in one case for the incredible period of eighteen years. Dr. Jost, however, had not treated the patient all of that time. The majority of these patients it seems were cured or greatly benefited, or, as the author expresses it, "the infection was vanquished in a majority of the cases." In his earlier experience failure was attributed to the fact that the vasa deferentia were not both treated at the same time. Some of the patients, in whom a single side was treated, refused to have another operation later. Attention was also called to the importance of treating deep urethral lesions as well as the seminal tract.

R. W. Staley³ is another who reports excellent results from vasotomy and irrigation of the vesicles, especially in those cases in which the secretion obtained by massage contains much broken-down tissue as

¹ Urological and Cutaneous Review, February, 1916.

² Transactions of the Chicago Urological Society, 1916.

³ Urological and Cutaneous Review, 1916, p. 131.

well as leukocytes. In properly selected cases, he considers the method curative.

L. T. Ashcraft,¹ of Philadelphia, speaks very highly of simple vasotomy in acute cases of seminal vesiculitis and expresses the opinion that it is not necessary to use injections through the opening in the vas except in chronic cases. He has found that drainage takes place through the opening and that pressure upon the epididymis is also relieved by this simple procedure. In his experience, even cases in which systemic symptoms were present improved under this treatment shortly after drainage became established, although in this class of cases he always injected 1 per cent. solution of protargol, or 5 per cent. solution of argyrol into the opening in the vas. He has rarely been obliged to give more than three of these injections. In discussing the major operations for chronic vesiculitis and its associated lesions, Ashcraft shows himself to be in accord with the authors previously cited, in that he believes that major operations should be reserved for cases in which all other measures have failed.

My own feeling in regard to these newer methods of treatment has not changed essentially since the subject was discussed three years ago. Up to the present time, I have not done either of the major operations for the reason that I have not seen cases in which the conditions seemed sufficiently distinct and urgent to warrant their performance. A number of intractable chronic cases which have long been under treatment are now being considered as possibly proper ones for vesiculotomy or, perhaps, even vesiculectomy. Acute cases and many chronic ones have done so well under the more conservative forms of treatment, supplemented by vasotomy and argyrol injections, that I have not had occasion to perform a vesiculotomy for their relief. Neither have I had any joint cases which in my opinion demanded a vesicle operation, although there is no doubt that some such cases are particularly favorable for operation, especially in view of the truly brilliant results which Fuller has reported.

In the discussion of the subject in Chicago, Lower,² of Cleveland, summarized the whole subject most admirably by stating that if the end-results in any considerable number of cases prove to be as good as they seem to be from early reports, then a great advance has certainly been made in the treatment of these rebellious cases, but that after all we must not deceive ourselves by allowing enthusiasm for operating to obscure the ultimate postoperative results.

With regard to the use of *vaccines* in these conditions, I have been very much impressed by opinions expressed within the last two or three years relative to the very slight, if any, benefit which can be expected from

¹ New England Medical Gazette, January, 1916.

² Transactions of the Chicago Urological Society, 1916.

them. There does not seem to be nearly as much enthusiasm expressed of late as there was a few years ago, and the present trend of opinion is entirely in accord with the results of my own experience with this form of therapy. I can state unhesitatingly that I have never treated a single case of gonorrheal infection of any kind in which there was positive evidence that any benefit resulted from the use of these substances. My experience with serum, however, has been different, and I believe that its administration in large doses has a decided effect upon severe systemic disturbances resulting from prostatovesiculitis, and even in acute joint involvement. Contrary to the experience of most surgeons, I have had better results from it in acute arthritic involvements than in the chronic forms.

In this connection it may be interesting to note that F. Maletterre¹ reports excellent results from the use of this serum in the joint complications of gonorrhea. He injects from 20 to 30 c.c. at the first dose, and then decreases the quantity at each subsequent injection. If the patient becomes sensitized to the serum, however, larger doses should be given if their use is continued for any length of time, and the intervals between the injections be lengthened.

The best results are to be expected in cases of multiple joint involvement accompanied by fever but with only moderate local symptoms.

An excellent result is reported by Bendell and Mount,² of Albany, from the use of a stock vaccine in a case of colon bacillus vesiculitis. The patient was a young man, aged twenty-one years, who complained of vesical irritability and painful and frequent urination. There was no history of venereal disease, nor of any mouth or throat affection. Examination of the urine showed many pus cells, red-blood corpuscles, and microorganisms. Cultures gave a profuse growth of colon bacilli. Some of the urine injected into a guinea-pig caused its death through septicemia within thirty-six hours. Rectal examination showed that the right lobe of the prostate was considerably enlarged and that the vesicle on that side was easily palpable. Both prostate and vesicle were sensitive to touch. Five bacterin injections were given, the initial dose being 17,000,000 and the dosage being progressively increased up to 62,000,000. Improvement followed the first injection. About two weeks after the injections were stopped, a specimen of urine obtained by catheterization was injected into a guinea-pig for the purpose of seeing whether tuberculosis would develop, provided the animal did not develop septicemia and perish from it. At this time the urine was negative microscopically, containing neither pus cells nor spermatozoa. The result of the guinea-pig inoculation proved negative.

In looking over the literature of this subject, the authors were struck

¹ New York Medical Journal, May 27, 1916.

² American Journal of Surgery, May, 1916.

with the paucity of cases reported, and while they appreciate that the report of a single case possesses no great scientific value, they still consider their case sufficiently interesting to warrant publication.

II. B. Culver¹ reports the result of his bacteriological studies of the prostatic secretion and contents of the seminal vesicles in the cases of 34 patients, 26 of whom were affected with subacute or chronic joint involvement. None of these patients had had any urethral discharge for at least six weeks, and the greater number had not had any for a number of months or even years, and a few of them had never had urethral discharge. In every one, however, there was clinical evidence of inflammation of the prostate or seminal vessels. The secretions were obtained by different methods, the object of all of which was to guard against contamination from other parts of the urinary and genital tract. Pyogenic organisms were obtained in 70 per cent. of the cases, a great variety being both aërobic and anaërobic. In 66 per cent. of the patients the organisms seemed to be specific for the individual, as shown by the occurrence of a positive reaction after the injection of autogenous vaccines. Their action was most variable, but, as a rule, consisted of slight chilliness followed by a little rise of temperature and the development of headache and anorexia. The earlier the reaction appeared, the more severe it seemed to be. The development of transitory urethral discharge was also noted as one of the phenomena following the injections, and likewise exacerbation of the joint symptoms. As some of the patients showed marked improvement after the injections, their use was continued as a therapeutic measure in conjunction with massage of the prostate and vesicles, irrigations, and the administration of drugs. As a rule, 6 of these therapeutic injections were given. In 5 of the 12 cases thus treated, negative cultures were obtained from the secretions after periods varying from six weeks to three months, the average being ten weeks. Five others, although still having positive cultures at the time the report was made, have improved considerably in health.

An important point which the author brings out is that in many cases a single examination of the prostatic and vesical secretion will apparently show it to be non-infectious, whereas repeated examinations will reveal pyogenic microorganisms.

Schmidt's findings are practically the same as those of Culver.

In the discussion which followed the Chicago symposium an excellent point was made by Dr. Smith, of Cincinnati. He stated that before performing vesiculotomy on the living subject, he did it several times upon the cadaver, and that he would recommend that other surgeons do likewise. To one who has dissected out the vesicles through the perineal incision, particularly for the purposes of demonstration to undergraduate or post-graduate students, as it has fallen to my lot to do many

¹ Journal of the American Medical Association, February 19, 1916.

times, the importance of this suggestion will be apparent. It is a difficult procedure; and the occasional operating surgeon will find that he cannot do these operations with the skill and expedition of such past masters as Fuller and Squier, for instance. Smith states that he would hesitate to do an operation of such magnitude in cases in which neurasthenic symptoms predominated, reserving it rather for the pus and joint cases, in which evidence of the relation existing between the vesicles and the symptoms present is more plain. Surely this is good advice.

Tumors of the Testicle. Three cases in which the x-ray has been used with success in the treatment of tumors of the testicle have been reported by Beclere,¹ who expresses the opinion that neoplasms originating in this organ are more favorably influenced than those in other parts of the body owing to the marked sensibility of the testicular tissues themselves to the rays. The first case in which he used this form of therapy was that of a young man who previously had a retained testicle removed on account of pain and epitheliomatous degeneration. Within three years from the time of the operation, he had developed a large tumor of the spleen, and at the time he came under observation was much emaciated and very anemic, although there were no signs of leukemia. The tumor filled the entire left half of the abdomen and extended somewhat over to the right side. After five months' treatment, the abdominal mass had disappeared and the patient had regained his normal weight. During the five years which have elapsed since the treatment was discontinued, there has been no recurrence of symptoms. Permanent cure was also obtained in one of the other cases, but the remaining patient, though benefited locally, eventually succumbed to metastasis.

Three cases of *malignant disease of the testicle* have been reported by W. P. Willard.² In the first case, operation was done about two months after the appearance of the tumor; and in the second, six months thereafter. The third case was operated upon twenty-one months after the appearance of the tumor. In the first case metastasis to the lumbar glands became apparent within five months from the time of the operation. In the second case, local recurrence took place eighteen months thereafter. In the third case, the patient was well four months after the operation. These cases illustrate the serious prognosis which should always be given in cases of this kind. With reference to removal of lumbar lymph glands in operations for removal of neoplasms of the testicle, I wish to call attention to the technical difficulty of the procedure, and also to the circumstance that it is quite probable that glands situated so high up that they cannot be satisfactorily reached are also involved at the same time that the inferior lumbar nodes are diseased.

¹ Bulletin de l'Académie de Médecine, July 25, 1916.

² California State Medical Journal, 1916, p. 134.

It may be that these glands are not palpably enlarged; but considerable experience at the autopsy table has taught me that it is quite possible to have slightly enlarged pre-aortic glands which would entirely escape detection, even through any of the extensive incisions employed in the modern operations for removal of the testicle and its associated lymphatics.

In this connection another case reported by Outland and Glendenning¹ is of interest. It was that of a man, aged fifty-five years, who had had an abdominal tumor for fifteen years which, during the six months previous to the time that he came under the author's observation, had increased so rapidly in size that it filled the left upper quadrant of the abdomen. Upon operation, it proved to be a cyst filled with chocolate-colored fluid. It was so large and adherent that it could not be removed, so the fluid was evacuated and the patient sent back to bed. He succumbed to shock at the end of six hours. At autopsy, the cyst wall was found firmly adherent to the left kidney. The left testicle was absent. The authors concluded, therefore, that the cyst had originated from a retained abdominal testicle which had undergone degeneration. I have had 2 cases in which testicles so retained have undergone cystic change. Fortunately, they came to operation at a period in their evolution when their removal was possible.

A New Operation for Varicocele. Del Valle,² of Buenos Aires, describes a new operation for varicocele which has been perfected in Decoud's Clinic in the University in that city, and which he believes to be superior to any of the operations heretofore employed for this affection. He has treated more than 60 patients by this method, 20 of whom he has followed carefully for from two to four years after the operation. A complete cure was obtained in all but 1 of these cases, and the failure in that one was attributed to a technical error during the operation.

The operation is performed as follows: The external inguinal ring is exposed by an incision about 2 inches long. The cord is freed and its coverings carefully incised so that its component elements can be thoroughly separated from each other. All the veins are carefully dissected from the external ring down to the top of the testicle. They are then lifted forward out of the wound by the assistant, who holds each extremity of the bundle between the finger and thumb of each hand while the surgeon separates them into an anterior and posterior group, after which he places a catgut ligature around the posterior group a finger's breadth above the testicle. Next a silk ligature is placed upon the anterior group two fingers' breadth above the one applied to the posterior veins. The end of this ligature is left long. The next step consists in making an incision about an inch and a half long through the

¹ Surgery, Gynecology and Obstetrics, p. 204.

² Ibid., June, 1916.

aponeurosis of the external oblique muscle a finger's breadth internal of and parallel with the fibers of the internal pillar of the ring, passing a

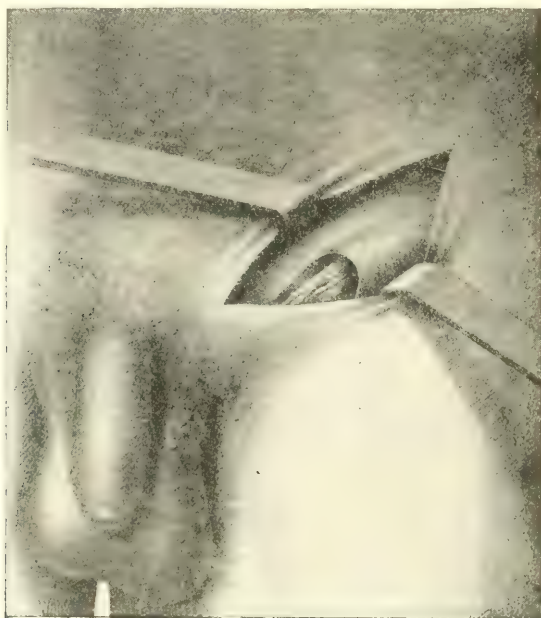


FIG. 33.—First step of operation.

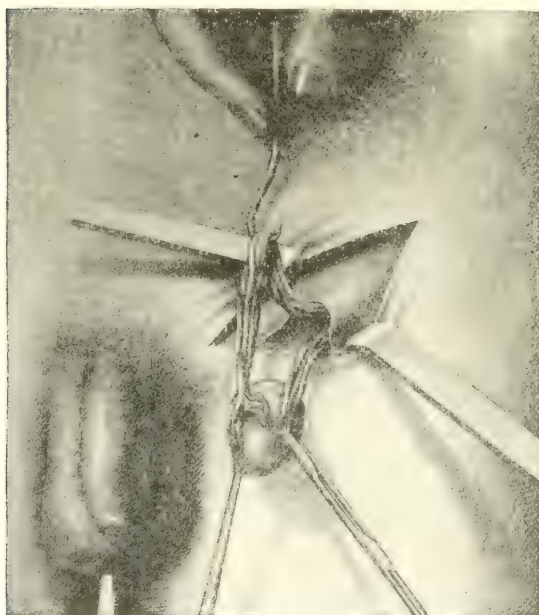


FIG. 34.—Second step of operation.

forceps through it and the underlying internal oblique and transversalis muscles, and then bringing it out through the ring, after which it is used to draw the silk ligature previously placed around the anterior group

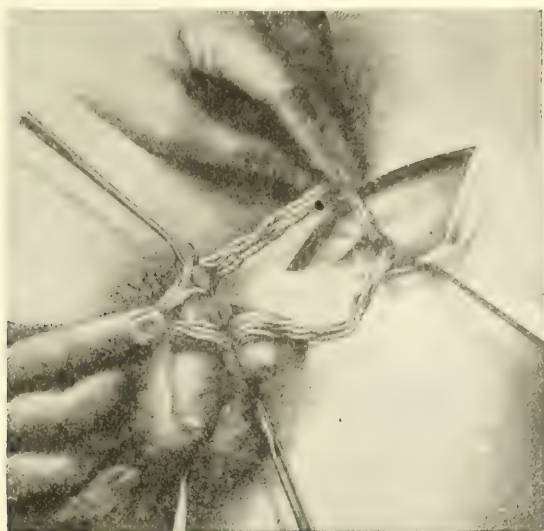


FIG. 35. —Third step of operation.



FIG. 36.—Fourth step of operation.

of veins up through the opening. The testicle is raised to the desired position and then the end of the silk ligature is threaded on a needle, passed through the aponeurosis of the external oblique, and tied. The

operation is completed by sewing the flaps of the fascia together behind the loop of the veins so as to leave each end of the incision open, and

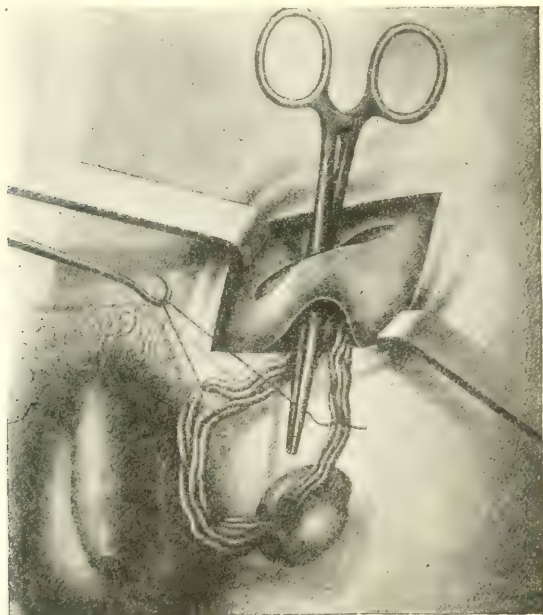


FIG. 37.—Fifth step of operation.

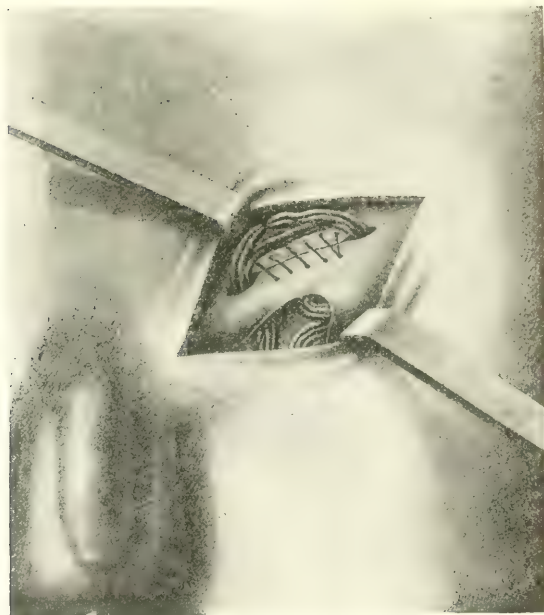


FIG. 38.—Sixth step of operation.

thus protect the veins from constriction. If the posterior group of veins is dilated instead of the anterior group, the opening in the aponeurosis of the external oblique muscle is made parallel with the external pillar instead of the internal.

Anatomical studies have shown that there is an anastomosis between the anterior and posterior veins of the pampiniform plexus, and the author believes that when the circulation through the two groups of vessels is interfered with at different levels, the blood current will be forced through the collateral veins connecting them. Thus the circulation of the cord will not be materially interfered with, but merely transferred to collateral vessels. He also believes that the transplantation of the veins between the muscles of the abdominal wall lessens their tendency to further dilatation. Figs. 33 to 38 make plain the technic of this operation which is, at least, interesting.

Another paper has been written by Tourneux concerning the advisability of the inguinal route in the operation for hydrocele. This method, first suggested by Gomoiu and Phocas, consists in forcing the testicle together with the hydrocele out of the scrotum and into an incision made in the groin above Poupart's ligament. After the fluid has been let out of the sac by puncture, the testicle and its coverings are drawn through the wound, and treated as the operator deems advisable. Then the testicle is pushed back into the scrotum and the wound is closed.

THE PENIS AND URETHRA.

Chancroid. With the exception of the very common inguinal adenitis which accompanies chancroids, the text-books make little mention of complications due to transmission of the virus through the lymphatics, the majority of them limiting their remarks to an allusion to a lymphangitis affecting the dorsal vessels of the penis. The development of one or more circumscribed nodules along the course of these vessels is not uncommon, and it is not very unusual for them to undergo rapid supuration to open and then to become converted into deep ulcerations. In some cases, however, probably the majority, they undergo rapid resolution. In all likelihood these lesions are due to infection with the bacillus of Ducrey, which passes directly along the lymphatic vessels.

A less common complication has recently been described by Radaeli.¹ It consists in the formation of abscesses in the coronary sulcus and is believed by the author to be due to invasion of the coronal lymphatic plexus by the streptobacillus of Ducrey, which reaches it in the same way as it reaches the larger lymphatic channels on the dorsum of the

¹ *Giornale Italiano Delle Malattie Venerel*, E. Della Pelle, February 16, 1916.

penis. This plexus extends from the plexus of Panizza, which is situated upon either side of the frenum, and encircles the base of the glans. The author's observations lead him to believe that the site of the abscesses in this region frequently correspond to the point at which a channel is given off to pass upward along the dorsum. This supposition accounts for the pyriform shape of the primary infiltration. In 2 cases he recovered the streptobacillus from the contents of the abscess, it being the only microörganism obtained by culture.

The symptoms and course of this complication are described as follows: The lesion begins as a small nodule deeply situated under the mucous membrane of the sulcus, which it pushes up more or less. It is larger at the base than at the top, being somewhat pyriform in shape, as already stated. In its first stage it is indurated throughout, although after a few days the central portion becomes soft and is transformed into a little abscess which opens spontaneously. After opening, it may either undergo spontaneous healing or become deeper and more extensive as to surface area if ulceration of the surrounding tissue takes place. Failure to heal is attributed to a secondary infection with the streptobacillus of Ducrey, transferred directly from the contiguous primary lesions. Because of this rapidity of evolution, the author expresses the opinion that these little metastatic abscesses may escape attention when they heal spontaneously, or, if healing does not take place rapidly, may be mistaken for new chancroidal lesions developing as a result of direct contact with other sores. He thinks that the complication is not as rare as it might at first thought be considered.

As to *prognosis* and *treatment*, the following considerations are of importance. In cases in which the complication develops late in the course of an attack of chancroid, after the virulence of the infecting organisms becomes reduced, spontaneous healing after rupture should be considered the rule. In cases in which it develops during the more virulent stages of the disease, ulceration and considerable destruction of tissue are probable, and cure is likely to be long delayed. In the first class of cases protection of the margins of the ulcer is recommended, together with the observation of cleanliness and the use of simple applications. In the latter class, disinfection with hot strong antiseptics and cauterization of the raw surfaces in conformity with the indications present in the individual case are the measures from which the most good is to be expected.

Fibromyoma of the Prepuce. Benign tumors of the integuments of the penis are rare, and, with the exception of papillomata, the prepuce is hardly ever the seat of such neoplasms. A few cases of cystic tumor, lymphangioma, and fibromyoma have been reported, the latter being both single and multiple. Such growths do not give rise to any trouble until they attain sufficient size to interfere with the function of the organ, or until they undergo ulceration. Their greatest importance is

probably due to the circumstance that they may undergo sarcomatous degeneration, as has been shown by various authors who have studied this subject.

Rapid increase in the size of a tumor which has been present a long time should lead one to suspect such metamorphosis, and especially so, according to Bramann, if there be an associated infiltration of the surrounding tissues which, by exerting pressure upon the urethra, makes micturition difficult. It seems that ulceration of benign neoplasms is not in itself any indication of malignancy, being due rather to poor nutrition of the skin, pressure, or traumatism.

A case of fibromyoma affecting the prepuce was recently reported by Delfino,¹ of Genoa. It was that of a man, aged forty-nine years, who, at the age of eighteen, was affected with a hard chancre, upon the scar of which there developed a small indurated and movable nodule the size of a grain of wheat, which caused him no inconvenience whatsoever. During the subsequent years this nodule developed very slowly until it attained the size of a cherry. Three years before the patient came under observation, he noticed that the tumor began to grow more rapidly than it had before. At the time that it was first seen, it was as big as a large nut. A month previous, the surface had become ulcerated at three different sites. The tumor was hard and fibrous throughout, was freely movable, and was not painful to touch. Careful examination failed to reveal any similar growths in other parts of the body. There was no interference with urination, and an exploration of the urethra did not show any contraction. Wassermann reaction was positive.

In view of its slow development, its movability and the freedom from infiltration of the inguinal lymph nodes, a diagnosis of fibroma was made and the tumor removed under local anesthesia. Upon microscopic examination, it was found that the tumor was composed of numerous smooth muscle fibers arranged in bundles and held together by a capsule of connective tissue which separated the fibers from each other. The skin covering the tumor in the region of the ulcerations did not show any changes except those due to inflammatory infiltration. There was considerable hypertrophy of the muscular tunic of the blood-vessels similar to that described by different pathologists as occurring in fibromyomata in other parts of the body. Inasmuch as the tumor had developed in a syphilitic, sections of it were stained for the *Spirocheta pallida* by the Bertarelli-Levadite method, but the result was negative.

Primary Carcinoma of the Urethra. In this review for 1913, a case of primary carcinoma of the male urethra localized in the fossa navicularis was reported, and a short review of urethral carcinoma was made. The investigations of Karika, who found that the two sexes are affected with practically the same frequency, were alluded to. A case recently

¹ Journal d'Urologie, September, 1915.

reported by George Erety Shoemaker,¹ of Philadelphia, is particularly interesting, inasmuch as it was treated with radium, owing to the fact that it was practically inoperable at the time the patient came under observation. It occurred in a negress, fifty years of age, who applied for treatment because of retention of urine. She had had difficulty in voiding for about five months prior to her admission. Upon examination, it was found that the urethra and peri-urethral tissues were so infiltrated with nodules that even the smallest urethral catheter could not be passed into the bladder. Consequently, resort was made to a No. 6 ureteral catheter which, after some effort, was passed and secured in the bladder so as to permit gradual drainage. After a few days of this continual catheterization, a No. 12 soft catheter was substituted for the ureteral instrument.

It occurred to Dr. Shoemaker to try the effect of radium in this case, and between December 14, 1915, and January 4, 1916, nine applications of three hours each were made. On December 24 a few drops of urine were voided spontaneously. Micturition improved each day until, on January 15, the patient was able to completely empty the bladder. At that time a No. 19 flexible catheter could be used. The patient considered herself well and refused to have an operation for removal of the inguinal lymph nodes, which, however, were not enlarged, although Dr. Shoemaker advised their removal. Like many of her race, this patient failed to return after being advised to have an operation.

Microscopic examination of a piece of tissue removed from the meatus showed that it was a squamous-cell carcinoma.

The High-frequency Current in the Treatment of Urethral Lesions. Ballenger and Elder,² of Atlanta, report successful results from the employment of Swinburne's method of treating chronic urethral folliculitis by fulguration with the d'Arsonval current. The method consists of introducing a tiny bulbous electrode directly into the diseased follicle and applying the current from two to ten seconds. The tissues become white within a few seconds and slough off in from two to three weeks.

McCarthy's improved cystourethroscope is used and an electrode is then introduced through a urethral catheter. A 22-gauge silver wire bulb at the distal end serves admirably as an electrode. When the wire protrudes from the catheter at the desired length, the proximal end is fixed to the catheter by means of adhesive plaster to prevent any slipping. A small rubber cap is placed over the electrode to prevent the irrigating solution from spraying in the surgeon's face. This treatment, of course, is applicable only to chronic cases and should be combined with proper treatment of any associated lesions, such as involvement of the prostate or seminal vesicles.

¹ Surgery, Gynecology and Obstetrics, June, 1916.

² Journal of the American Medical Association, May 27, 1916.

Granville MacGowan¹ also calls attention to the value of the high-frequency current in the treatment of polypoid and papillomatous growths in the posterior urethra. In one case he found the entire posterior urethra blocked with these little growths, the symptoms which were produced being those of progressive prostatism. The growths were removed with the cautery, after which it was found that there was some contraction of the vesical neck by a fiber-like mass projecting out over the floor of the urethra. With some difficulty this obstruction was removed by use of a punch and a rongeur. A month later examination showed that an adenoid was growing directly in the centre of the channel that had been made, originating presumably in one of the glands of Albarran.

In discussing the etiology of these growths, MacGowan expresses the opinion that they originate the same way as papillomata on the external genitals through the laying bare of papillomatous bodies by slight injuries in the presence of the favorable elements of heat, moisture and chronic infection. He divides polypoid growths into two classes, namely: the soft or mucoid, and the fibroid. The first class have but a single bloodvessel with one layer of flat epithelium, the bloodvessel being surrounded by a stroma so delicate that it is negligible. Consequently, they respond quickly to the action of the cautery, so that a single spark from the high-frequency current, or a touch from the electric cautery, will destroy them. Those of the second class are better organized. The central bloodvessel may be single or branched, and is surrounded by a well-defined stroma, which is covered by at least two layers of squamous epithelium. When viewed through the water distention urethroscope, this type is not so translucent as the mucoid variety, nor is it as easy to destroy unless it is severed by the cautery knife, or unless the central bloodvessel happens to be coagulated by the spark upon its first application. These fibrous polypoid growths are most frequently found on the lateral walls posterior to the verumontanum. With reference to true papillomata, the author states that he has found them frequently in front of the colliculus. These latter are generally difficult to cure, frequently resisting the action of the cautery for weeks before they finally yield to its destructive power.

Cysts of the posterior urethra were referred to in this review some years ago, and doubt was expressed that their mere presence might account for the symptoms complained of in some of the subjects in whom they were observed. It seems that further investigation is necessary to determine their true pathological rôle if they have any. In MacGowan's experience these cysts have been very easy to destroy with the newer caustic methods. Of course, if they be large enough to produce obstruction of the vesical outlet, it is readily understood that they may be responsible for the symptoms.

¹ Journal of the American Medical Association, September 18, 1915.

MacGowan's associate, Robert V. Day,¹ has discussed the technical method of dealing with these growths. He finds that different instruments will be applicable to different cases. He has used a non-flexible insulating material which consists of a silica tubing having the diameter of a No. 11 French catheter. One end is fitted into a groove with a pistol-shaped handle made of vegetable fiber and held firmly in place with a set-screw. Through the top of the handle, and extending on through the bore of the silica tubing, a piece of piano wire is passed, the distal end being sharpened to a fine point. The excess of wire is bent over the handle into a small loop to which the high-frequency connecting cord is attached with a watch-chain snap. The manner in which this simple instrument is used is much like that by which skin growths are destroyed by the electrolysis needle, except that in these urethral cases the incisions are made parallel. This insulated needle may be inserted through any open endoscopic tube.

New Growths of the Prostatic Urethra in Relation to Tuberculosis. P. S. Pelouze,² of Philadelphia, publishes an interesting paper based upon 9 cases which came under his observation in the Jefferson Hospital, in all of which there were peculiar growths in the posterior urethra, and evidences of associated tuberculosis were generally present. The growths were located principally upon the roof and lateral walls of the prostatic portion of the canal, being most numerous just external to the vesical sphincter. They varied in size from about one-half to one-quarter that of the average normal verumontanum. They were lighter in color than the surrounding mucous membrane, usually occurred in clusters, were very slightly pedunculated or sessile, and in no way resembled urethral papillomata. Although they appeared to be solid during the earlier stages of their development, some of them evidently underwent cystic degeneration later, so that when ruptured they discharged a thick white substance. Sections of the solid growths proved to be lymphoid in character. As the author has never found such growths in patients who did not present signs of tuberculosis, he believes that their occurrence warrants one in making a diagnosis of tuberculous disease, unless most careful examination of the various organs of the body fails to reveal any trace of that disease. In none of the cases could any marked change in the shape and consistence of the prostate be detected by rectal examination; consequently, it is probable that the new growths do not penetrate any considerable distance beyond the urethral mucous membrane overlying the gland. It is interesting to note that none of the patients voided a cloudy urine. In all but one case, however, shreds were present, though there were hardly any pus cells. A fairly constant symptom was continuous burning pain at the

¹ Journal of the American Medical Association, November 20, 1915.

² New York Medical Journal, October 16, 1915.

neck of the bladder and pain at some point in the anterior urethra during urination.

J. F. McCarthy,¹ of New York, also calls attention to the importance of carefully examining the deep urethra in cases of genito-urinary tuberculosis, and reports cases of unilateral renal tuberculosis in which there were associated urethral lesions.

¹ Surgery, Gynecology and Obstetrics, 1916, p. 330.

SURGERY OF THE EXTREMITIES, SHOCK, ANESTHESIA, INFECTIONS, FRACTURES AND DISLOCATIONS, AND TUMORS.

By JOSEPH C. BLOODGOOD, M.D.

SHOCK.

War Neuroses. Psychic Shock. The most interesting reports in recent literature come from the military surgeon. Oppenheim¹ entitles his contributions "War and Traumatic Neuroses." He calls attention to his statement in 1889, when he said that there may be an injury to nerve tissue sufficient to influence function, yet not producing enough cellular change to be recognized under the microscope. This statement created a great deal of opposition. Many of his opponents called his traumatic neuroses "indemnity" hysteria. Oppenheim is of the opinion that the present war has vindicated his view and established traumatic neurosis on a scientific basis.

Bonhöffer² does not go as far as Crile with regard to the relation between the mental disturbances due to the war and subsequent insanity. Nevertheless, he is of the opinion that the severe emotional strain will have its effect both upon the nervous system of the soldier at the front and the people at home. We must also bear in mind that this factor may light up latent mental tendencies or dispositions. Bonhöffer is of the opinion that there is no psychosis peculiar to the war. He has been able to find no evidence that the real and advanced mental diseases have been increased by the war. Apparently, his address is more an expression of opinion than the disclosure of any new facts.

Jensen³ maintains that pain, worry, and other unpleasant emotions act the same as the so-called operative shock. Their chief influence is on the splanchnic nervous mechanism, with paralysis of the vaso-constrictors. This affects the entire intestinal canal, the chief feature of which is paralysis—dilatation of the stomach, gas distention. Whether it is an acute or chronic condition, continuous or recurrent, this intestinal stasis interferes with the defensive mechanism of the

¹ Berl. klin. Wehnschr., March 15, 1915; review in Journal of the American Medical Association, 1915, lxiv, 1533.

² Journal of the American Medical Association, 1915, lxiv, 163.

³ Lancet, 1915, clxxxviii, 231; review in Journal of the American Medical Association, 1915, lxv, 33.

mucous membrane, and toxins pass into the circulation. In this way, we have established a vicious circle. Of course, there is nothing new in this idea, but many so-called intestinal intoxications are secondary and not primary, and in many of these cases psychic influences are more beneficial than treatment directed to the intestine only.

Patrick¹ discusses with great clearness the factor of fear in nervous cases (functional nervous disorders), and divides them into different groups. He reports cases in detail.

Personally, I have seen the blood-pressure fall from 160 to 80 from fear alone.

Every military surgeon has seen extreme degree of shock without any demonstrable lesion. Some of these may be due to concussion and not fear, just as we know that the nerve trunk may be markedly disturbed by concussion without laceration.

Crile has contributed numerous books and articles on the kinetic theory which has chiefly to do with the relation between emotion, shock and acidosis.

Cannon has recently written quite extensively on the relations between emotions and shock.

It is my opinion that the relations between fear, emotions and other mental disturbances, and the general condition called shock are well established. The most common postoperative discomfort are gas pains, with and without distention. This temporary paralysis of the alimentary canal is the first result of any of these emotional disturbances. The two conditions have enough in common to be considered together. War neuroses, therefore, begin as cases of psychic shock.

General. Before mentioning some of the new contributions which have appeared during the past year, I find it interesting to briefly summarize an article on shock under the heading "Therapeutics."² In the introduction, it is stated: "With correct knowledge of shock, treatment should be more rational." Then it is added: "Unfortunately there are differences of opinion, both as to the physiological and pathological changes which occur during shock, and for this reason the many advocated treatments confuse the therapy."

When the clinical picture of shock is described, blood-pressure is not mentioned. From a surgical stand-point, of all the signs and symptoms in this very complex condition called shock, the blood-pressure is one of the most exact signs helpful to us in prevention, recognition and treatment. It seems to me that it is confusing to try to differentiate shock from collapse.

Then they mention the usual various theories under the headings "Crile's Kinetic Theory," "Acapnia (Henderson)", "Suprarenal Exhaust-

¹ Journal of the American Medical Association, 1916, xlvii, 180.

² Ibid., lxvi, 1464.

tion (Corbett)." Seelig and Joseph have apparently no theory, but their experiments prove that paralysis of the vasomotor center is not the primary cause of the other symptoms of surgical shock. When we come to the discussion of therapeutics, they mention Hogan's colloidal gelatin.¹ Apparently this latter method is given chief space because it is most recent. They, however, mention the well-established older methods. First, saline subcutaneously, per rectum or intravenously; with the rectal infusion, black coffee. Then they advise Corbett's epinephrin solution, which is given with the saline. For pain, morphine is advised. When there is acute anemia of the brain, lower the head of the bed, put bandages around the limbs and abdomen and apply hot-water bags. Strophanthin may be given intravenously (if the patient has received digitalis recently this drug is contraindicated). Camphorated oil hypodermically; strychnine, gr. $\frac{1}{30}$, which should not be administered more than once in six hours; ergot intramuscularly once in six to eight hours; pituitary extract. These drugs are supposed to be helpful in raising the blood-pressure. Small amounts of hot liquids by mouth. If there is perspiration, atropine (in my experience patients in shock do not perspire). Hot-water bags are much better for cold perspiration than atropine. Then it is urged that no drug should be pushed too far, nor should many drugs be given at the same time.

I have been attempting to give a yearly review on shock for the past sixteen years, and I can appreciate the difficulty confronting the writer on "Therapeutics" in the *Journal*. But if a young surgeon read this article on shock, he would really not know what to do first, or in what order.

When I finish a brief review of the literature, I will give again a working method which I personally employ in the prevention and treatment of shock.

Operative Shock. Surgeons are most interested in the shock which may occur during or after operation, because we are beginning to learn that this form of shock is more or less under our control. The factors which have produced shock in an accidental injury are not under our control, and we are compelled to treat the patient as we find him, but in operations it is different, and here, when it is possible, the best treatment is really not treatment of shock at all, but to so prepare the patient, direct the anesthesia, and execute the planned operation that if there is any shock at all, it will be easily combated by simple therapeutic measures. Personally, during the past year I have not given a single drug hypodermically for shock, and I find that I have given intravenous salt less than in any previous year. In the great majority of cases the treatment has not gone beyond the Trendelenburg position,

¹ Journal of the American Medical Association, February 27, 1915, p. 721.

the application of external heat, the subcutaneous administration of saline, and hot saline with coffee *per rectum*, and, perhaps most important of all, the patient is kept quietly in this position on the operating table until we feel, from the change in the blood-pressure and pulse, that he can be transported to the ward with safety.

We may contemplate operative shock in three stages—before operation, during operation, and after operation. I am inclined to think that, as far as the surgeon is concerned, he can most readily control the condition during operation.

PREOPERATIVE TREATMENT. In my own recent experience with exophthalmic goitre, I have reduced the mortality to nothing by preoperative treatment. I cannot see any improvement in the operative technic, but these cases are given absolute rest in bed until their condition is such that the operation can be performed with a minimum amount of risk, and, so far, there has been no mortality. During this period, two patients were taken from my clinic to other hospitals, because I would not consent to operate until there had been a longer period of rest, and were operated upon within a few days. Both patients died on the table, or within a few hours, and I know that in these two cases the anesthesia and the surgery were good. The fault was with the judgment as to the time of operation.

In general, the better the condition of the patient, the less the danger of shock, but we cannot always have this advantage. Patients will come for surgery late, depressed by the disease and by fear and anxiety. Naturally, any investigation which will help us to improve the general condition of the patient is of the greatest importance. In every case we have to use our judgment and decide between the danger of putting off the indicated operation, and the danger of immediate operation without any preparation. When operation is not indicated at once, no harm is ever done by a few days' delay for preparation. Young has demonstrated this with his most painstaking preliminary preparation for perineal prostatectomy. A. C. Burnham¹ is of the opinion that the administration of *glucose solutions* has a definite prophylactic action against operative shock. If there is no contraindication for food by mouth, he gives a meal of bread and cereal eight hours before operation and 100 to 200 calories (6 ounces of coffee, or orangeade with 1 ounce of lactose) three hours before operation. If food cannot be given by mouth, he recommends an intravenous administration of a 5 per cent. freshly prepared glucose solution, or subcutaneously 2 or 3 liters of 5 per cent. solution, or *per rectum* 1 or 2 liters of a 5 per cent. glucose solution in tap water.

I frequently use the rectal method before operation, but save the subcutaneous infusion for the operating table. It begins with the

¹ American Journal of Medical Sciences, 1915, cl, 431.

anesthesia. Lane uses this practically as a routine when he resects the colon. This glucose treatment can be continued after operation.

I am inclined to think that we are apt to leave the treatment of expected shock until after the operation is begun or finished. We generally know in what cases shock may be expected. In the past, we have concentrated our attention on the second and third stage, and it is my opinion that we should pay more attention to what can be done by way of preparation of the patient for an operation in which we know there will be a large element of shock. I am confident that many patients are depressed by catharsis, weakened by starvation, and their tissues dehydrated by neglect to give them plenty of liquids, and in some cases they are doped with narcotics, so that they will sleep the night or two before operation, or come to the operating room more or less stupefied. It is quite true that some group of patients may best be prepared by catharsis and starvation, but no rule will apply to all. Some form of sugar and bicarbonate of soda is being added to our saline solution. I wish I were able to know how much good the sugar really does. I think our evidence in favor of the fluid is conclusive, and in some cases the evidence in favor of the bicarbonate is almost as good. But as to the sugar, I am not quite certain. When we really have an acidosis, I have found that we need more than sugar, and, of all the single foods, milk in some form gives the best results.

But not all acidoses are due to starvation, and acidosis is not always a condition necessary to treat any more than one would administer drugs to reduce fever. Some forms of acidosis are physiological. It is this knowledge that makes one skeptical of contributions similar to Burnham's, and at the present time we must not put too much reliance on any preoperative treatment which will be prophylactic against operative shock. So far as I know, there is no harm in the administration of the glucose solutions.

Guerry¹ advises thorough preoperative preparation: Morphine gr. $\frac{1}{6}$, and atropine gr. $\frac{1}{50}$ are given hypodermically just before the patient leaves for the operating room; the anesthetic is begun with nitrous oxide and changed to ether; the operative work should be bloodless and rapid; local anesthesia is useful only in selected cases, as Guerry is of the opinion that this prolongs the time of operation.

Those who use local anesthesia in combination with general, know that it does not prolong the operation time to any extent and that it reduces the amount of general anesthesia necessary for the completion of the operation. I will speak of this again when I discuss anesthesia.

Blood-pressure. For perhaps over five years we have recorded on a chart, during every operation at St. Agnes' Hospital, the pulse and blood-

¹ Journal of South Carolina Medical Association, 1915, xi, 226; review in Surgery, Gynecology and Obstetrics, 1915, xxi, 475.

pressure, beginning as a rule a few days before operation and for some days after it. The record is kept by the nurse under the direction of the anesthetist. In the column to the left of the chart, the condition of the patient is noted from time to time, especially as to color, whether he is struggling or not, vomiting, etc. In the column to the right, the operator dictates, from time to time, the nature of the manipulation. We are now having a copy made of these charts and studying them critically—it is a huge piece of work.

All the members of my staff agree with me that this chart has stimulated their interest in the relation of the different forms of anesthesia and the various steps in the different operations to the general condition of the patient as recorded on the chart and as reflected in postoperative convalescence and mortality. In the first three years, in the majority of cases, the general anesthetic was nitrous oxide and oxygen. In the past eighteen months, we have gradually returned to ether. In a large per cent. of the cases, local anesthesia has been employed with the same details as if the patient were not under a general anesthetic, and, in the majority of very handicapped cases, local anesthesia has been employed alone, or in conjunction with a slight amount of ether, never to the point of full narcosis.

The remarkable thing is that, since the experience with gas, we have found that with the return to ether our records seem to show results about the same, whether we have employed ether or gas, but all the results seem far better than before the employment of the charts. The only factors that I can discover to explain this are, first, the general anesthetic, no matter which, is better administered; that is, we have trained our staff to be better anesthetists; second, we have all concentrated our attention on the manipulations which produce shock and have attempted to avoid these manipulations, or to shorten their period; and perhaps the most important factor of all is the routine employment of novocaine 1 to 400 as a local anesthetic.

In addition, I am beginning to feel that changes in the blood-pressure are often at first physiological and not pathological, and that, in view of our ignorance of its exact mechanism, it is a mistake to treat especially low blood-pressure with drugs.

When the blood-pressure is high, we now rarely use gas. There seems no good reason to increase the blood-pressure with this anesthetic when the operation can be done with ether, or in some few cases with chloroform, without raising the blood-pressure. Then, again, we are not startled into immediate action by low blood-pressure. Simpler means are always employed first. In the first instance, the patient's head is lowered; often this alone brings the blood-pressure back. Painful operative manipulations are discontinued, or attempts are made to block them with novocaine. The third procedure is subcutaneous saline; the fourth, hot saline *per rectum*. Intravenous saline has been

given less this year than ever before. I have also discontinued the intravenous use of strophanthin. As far as I can make out, the general character of the cases has been about the same, and there seems to be an improvement in the results. When the results are fortunately pretty good, it is difficult to note slight improvements. But from this observation all of us have concluded that ether, properly given, is just as good an anesthetic as gas and oxygen. There is no doubt that in some cases gas and oxygen is a pleasanter anesthetic; perhaps in a few cases it is a safer one. But I am beginning to feel that when we employ local anesthesia, ether is often a better and safer anesthetic than gas. The point, however, I wish to make is this: The keeping of anesthetic charts seems to be a definite factor in improving anesthesia, whether local or general, and in teaching and perhaps forcing the surgeon to watch every detail of the operative procedure.

The element of time has too large a hold on the minds of many surgeons. There is no doubt that rough, painful operative manipulations do less damage when they consume less time, but if the same operation can be performed without this trauma and loss of blood, the additional period of time need not be considered. In fact, it is less dangerous to take more time with the utmost care than to be rapid and reckless as to injury and hemorrhage. Then, again, deep narcosis is of itself a depressant. Anything to reduce the actual amount of the anesthetic is helpful. Local anesthesia undoubtedly accomplishes this. Explain the combination as you will, I am confident that the combination of local and general anesthesia is better than general anesthesia alone, and best of all are the results of local anesthesia alone.

I therefore review the recent literature on the action of drugs on the vasomotor centre more to urge caution in their employment. Even in desperate cases I am not sure that we have at the present time any drug to be depended upon.

Pilcher and Sollmann¹ state that the nitrites depress the vasomotor centre only indirectly. The fall in pressure is due to peripheral action. Strychnine, except in very large doses, is probably inactive. Epinephrine has no direct effect upon the vasomotor centre. This is also true of camphor. Chloroform, as a rule, is a direct depressant. Sparteine has apparently no effect upon the vasomotor centre. Strophanthus is a moderate stimulant, while digitalis is not. Ether does not affect the vasomotor centre, except perhaps as a very moderate stimulant, but, as the experimenters state, ether was never pushed in their work to the point of vasomotor paralysis. The active principle of the pituitary gland has but a slight effect, occasionally depressant, more frequently perhaps stimulating. Intravenous lactic acid apparently stimulates the vasomotor center.

¹Journal of Pharmacy and Experimental Therapy, January, 1915; review in Journal of the American Medical Association, 1915, lxiv, 540.

Sweet,¹ from the surgical research department of the University of Pennsylvania, gives an excellent collective review on the relation of the ductless glands to blood-pressure in surgery, with thirty references to the literature. He also refers to his previous article on the "Relation of Blood-pressure to Surgery."²

He expresses the opinion that surgical shock is a condition marked by gradual, persistent, progressive fall of blood-pressure, and that it is observed in its most characteristic picture after extensive crushing injuries without loss of blood, burns, high intestinal obstruction, acute hemorrhagic pancreatitis, etc. It is Sweet's opinion that the fall in blood-pressure is primarily due to the failure of the peripheral and not of the central mechanism, that is, in the musculature of the small peripheral arteries, and it might be expected that the ductless glands play a part.

One should read this contribution in the original. The only practical thing offered is that small amounts of adrenalin continuously administered in saline solution during operation are indicated.

Sweet apparently agrees with Seelig and Joseph³ in regard to the peripheral origin of shock, but he does not refer to their excellent experimental work which I have previously reviewed.⁴ This is probably due to the fact that he is dealing here especially with the relation to the ductless glands, and is not reviewing shock in general. He refers especially to the contributions of Cannon.

The advice of Sweet in regard to adrenalin agrees with that of Corbett⁵ who is also influenced by the writings of Cannon and Elliott.

Cannon's book, *Bodily Changes in Pain, Hunger, Fear and Rage* (D. Appleton & Co., 1915) has just come to my attention. It is an account of recent researches into the functions of emotional excitement. One will find in this book references not only to the previous work of the author and his associates, but to the most recent literature on this subject.

NORMAL BLOOD-PRESSURE. Lee⁶ reports on blood-pressure determinations, urine examinations and differential blood counts in 662 apparently normal male adults about the average age of eighteen, height of five feet eight inches and average weight of 143 pounds. The average systolic pressure was 120, diastolic 80. The diastolic pressure was much more uniform. Of the group of 85 cases, 12 per cent.

¹ Collective Review, Surg., Gynec. and Obst., 1916, xxii, abstr., p. 581.

² American Practice of Surgery, Bryant and Buck, ed. 1911, p. 1063.

³ Journal of Laboratory and Clinical Medicine, 1916, i, 283; review in Journal of the American Medical Association, 1916, lxvi, 771.

⁴ PROGRESSIVE MEDICINE, December, 1915, p. 211.

⁵ St. Paul Medical Journal, 1915, xvii, 655; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 212.

⁶ Boston Medical and Surgical Journal, October 7, 1915.

of the total, whose blood-pressure was over 140, 9 or 10 per cent. showed albumin in the urine. Of these 85 cases with higher blood-pressure, 7 had cardiac lesions, only 9 of them showed albumin in the urine.

Rowan¹ writes under the title "The Practical Application of Blood-pressure Findings." He begins his article with the remarks that many blood-pressure readings, as made in the ordinary way, are practically worthless. He describes the source of error or inaccuracy, and draws conclusions from 500 recorded cases. He is of the opinion that the diastolic record is much more important than the systolic. When compared with the study of Lee, we note that the results are about the same. Among his 50 examinations between the ages of twenty and thirty, the average systolic pressure was 125, the diastolic 81. Between the ages of thirty and forty, Rowan finds the averages 142 and 86, between the ages of forty and fifty, 156 and 89; between the ages of fifty and sixty, 183 and 88.

My own charts record the systolic pressure only, so that I cannot speak from a large experience with the diastolic.

The surgeon is influenced most by the rise and fall in the pulse and blood-pressure. I expect to be able to show, when my research is published, that when the pulse and blood-pressure have remained practically unchanged throughout an operation we never observe the symptoms of shock, and the postoperative course is, as a rule, devoid of such complications as acute dilatation of the stomach, gas distention, anuria, or pneumonia, and the convalescence to full recovery is more rapid. I am confident, however, that we have not reached by any means the full limit of what is possible with regard to the patient during an operation, and I propose to add other conditions to be observed on the blood-pressure chart. But I would advise those surgeons who have not as yet employed the chart to begin with the simple record of pulse and systolic blood-pressure.

Electric Shock. I began this review with a discussion of psychic shock, because the literature seemed largely concerned with this phase of the question as brought out by the experiences of the war. The literature on electric shock is brought up to date (1915) in the *Journal of the American Medical Association*, 1915, lxiv, 763. The latest report of the committee investigating resuscitation from electric shock was published² in 1914.

Traumatic Shock. We might consider under this term those cases of shock in which the trauma is an accidental one and not the result of an operation. In the first place, there is a large number of observations from the war in which the patients are shocked, but no gross injury from shell or bullet can be found. The majority are of the opinion that

¹ *Journal of the American Medical Association*, 1916, lxvi, 873.

² *Ibid.*, February 28, 1914, p. 724.

the condition is not psychic entirely, but that the explosion has transmitted its concussion effects through the air or ground to the individual. Harzbecker¹ analyzes four cases of hemiplegia due to air concussion from a bursting shell six to twelve feet away. He is of the opinion that in all the fatal cases without signs of external injury there is probably some hemorrhages into a vital centre.

Traumatic Asphyxia. L. B. Robertson² observed six cases in February, 1913. They were brought to the Bellevue Hospital from a motion-picture theater after the cry of "fire!" had raised a stampede. Some of the cases were unconscious immediately or shortly after the injury. In all of the cases there was cyanosis of the scalp, face, neck and chest down to the third and fourth ribs. The lips and tongue were swollen, and the mucous membrane of the mouth was also cyanotic. The cyanosis extended down the back to the middle of the scapula. On closer examination, there were scattered red areas of different sizes resembling petechial hemorrhages. Subconjunctival hemorrhage was a common and startling feature.

Robertson was of the opinion that the condition was produced by pressure about the abdomen and chest persisting sufficiently long to cause a cessation of respiration, but not long enough to kill the patient. Among the six cases, two died of pneumonia. None had signs of cerebral hemorrhage.

I will never forget my first observation of traumatic asphyxia. The man was unusually strong. He had been caught between the bumpers of two freight cars. For the picture of cyanosis in this case look at the colored illustration found with the contribution of Beach and Cobb,³ and you will note that the cyanosis did not extend either anteriorly or posteriorly, below the line at the junction of neck and chest. My patient was extremely shocked, but he was not unconscious, when I saw him about two hours or less after the injury. The compression had ruptured the right rectus and the right oblique muscle. Loops of intestine could be felt beneath the skin. At that time we thought the man was dying of internal hemorrhage; it was considered a hopeless case, and he was sent to the ward to die. Some four or five hours later the cyanosis had practically disappeared, leaving only points of petechial hemorrhage, as illustrated in the article of Braun⁴ and Wienecke.⁵ As the patient's condition was better, I decided to give him the benefit of the doubt. Under ether, I explored the abdomen. There was no hemorrhage into the peritoneal cavity, but both visceral and parietal

¹ Deutsche med. Wochenschr., November 17, 1914; review in Journal of the American Medical Association, 1915, lxiv, 185.

² Canada Medical Association Journal, 1914, iv, No. 6; review in Journal of the American Medical Association, 1914, lxiii, 60.

³ Annals of Surgery, 1904, xxxix, 481.

⁴ Deutsche Ztschr. f. Chir., 1904, lxxiv, 411.

⁵ Ibid., lxxv, 37.

peritoneum were intensely cyanotic, as much so as the face when the patient was first admitted. The ruptured muscles were repaired as well as possible in a short and rapid operation.

The patient recovered and lived for twenty-five years, but he always had to wear a bandage for the hernia. Apparently this is the only case in which the cyanosis of the abdominal viscera could be directly observed at the forced laparotomy.

The thing that has impressed me most in going over the literature on traumatic asphyxia since 1904, is that the observers have been so interested in the cyanosis and petechiae that they have left no records in regard to the relationship to shock. In my case the shock was the most marked feature, if one for a moment could forget the color of the patient. I am inclined to think that Robertson observed his patients earlier after the accident, and that was why he was able to see the cyanosis of the upper portions of the chest and back.

Flatulence and Shock. Crookshank¹ has written a most illuminating little pamphlet. I do not know whether we should call this medical shock, toxic or psychic shock, but he is chiefly interested in the significance of flatulency as an indication of an insult of some kind. This book should be read along with the last book of Cannon² and compared with the recent books and articles of Crile on the Kinetic Drive.

Miscellaneous Literature. I have been reading the literature on shock for this review now for seventeen years, and I am convinced that it has been a great factor in helping me in the development of all the things that go for the benefit of my surgical patients. Yet, when one looks back over this tremendous literature, one is quite certain that no one contribution stands out ahead of all the others, but good points come from many of the articles. In the following I shall have time only to indicate certain recent articles which should be consulted for special points.

Baumel³ speaks of the *importance of lumbar puncture in cases of nervous shock and wounds of the skull in war*. He found it not only of diagnostic, but of therapeutic, value. We must always recollect that the shock produced by the injury may be kept up by some of the results of the same injury. This is exemplified best in hemorrhage, in peritonitis following traumatic rupture of the intestine, in the intense pain when there is fracture or dislocation with pressure, in the cerebral compression from hemorrhage. At the present time, fortunately, there is always one or more members of a hospital staff familiar with the technic of lumbar puncture, so that Baumel's advice to perform lumbar puncture for the relief of pressure systematically, day after day, will be free from danger,

¹ Paul B. Hoeber, 69 East Fifty-ninth Street, New York, 1913.

² Loc. cit.

³ Lyon Chir., September, 1915; review in Journal of the American Medical Association, 1915, lxy, 1492.

but anyone with little experience with lumbar puncture should recollect that it is a procedure not devoid of risk.

Apparently no one has taken up with Hogan's *intravenous gelatin solution* referred to last year.¹ This treatment was chiefly recommended for toxic shock. In relation to the use of adrenalin, or epinephrine, we should turn to the experimental and clinical work of Corbett, of the University of Minnesota. Although the use of this drug was advocated by Crile many years ago, there has been a recent revival of interest, as shown in my previous remarks.

Davis,² in his contribution on *morphine* from the Department of Surgery of Rush Medical College, is probably inspired by Bevan.³ I have referred to the latter's paper in *PROGRESSIVE MEDICINE* for December, 1915, p. 214.

Davis, from his comparative studies, finds that morphine preceding local anesthesia adds nothing to the efficiency of the anesthetic, but causes postoperative nausea and vomiting in about 25 per cent. of the cases. The combination of morphine and atropine before a general anesthetic apparently has no good effect—it does not protect the patient from any of the dangers and discomforts. For this reason morphine should not be given as a pre-anesthetic drug. There is no objection to its use after operation for pain.

I have given up morphine with local anesthesia some time ago, and I am not at all convinced that it should be a routine procedure before a general anesthetic. The majority of anesthetists who give gas and oxygen seem to think that a dose of morphine about a half-hour before anesthesia begins is helpful.

I believe that Bevan and his associates are on the right track. They are breaking away from routine and attempting to find out the best anesthetic or combination of anesthetics for the individual case or for the special group.

Lancaster⁴ covers the entire ground of the *preparation of the patient for operation*, chiefly, however, for patients whose eyes are to be operated on. We note that he advises sedative drugs the night before for sleep, and rather favors the preoperative dose of morphine, except when the patient's coöperation is desired in operations upon the muscles of the eye.

Gunn and Martin,⁵ from their experimental work at Oxford University, find that, in addition to direct *heart massage*, when there has been sudden cardiac failure, there should be *intrapericardial injections of epinephrin or pituitary extract*.

Simpson⁶ calls attention to *right-sided hypertension of the heart* as a

¹ *PROGRESSIVE MEDICINE*, December, 1915, p. 213.

² *Journal of the American Medical Association*, 1916, lxvi, 252.

³ *Ibid.*, October 23, 1915, p. 1418.

⁴ *Ibid.*, 1916, lxvii, 253.

⁵ *Ibid.*, lxvi, 32, editorial.

⁶ *Ibid.*, 1915, lxv, 941.

postoperative complication. It is apt to occur in cases with myocarditis. Deep narcosis with ether, prolonged extreme Trendelenburg position, rapid intravenous saline injections precipitate and intensify the condition. It should be treated by elevation of the head of the bed, small doses of morphine, and cardiac stimulants.

I am confident that myocarditis is one of the most frequent causes of postoperative death in a group of very fat women who give a history of shortness of breath on overexertion. In this group the most dangerous operations are intraperitoneal. The patients will not stand deep narcosis, Trendelenburg position and a long, traumatic operation. My deaths have occurred after operations for postoperative hernia, combined abdominal and perineal operation for cancer of the rectum, and in one case of cholecystostomy for gall-stones. In all of these cases I knew of the complication, did everything I could to prevent the fatality, but failed. Death took place usually at the end of forty-eight hours, or on the third day, with continuous rapid pulse and low blood-pressure, typical air hunger as is sometimes observed in hemorrhage.

Buerger,¹ from his experience in military surgery, is of the opinion that *fat emboli* are much more frequent than the literature on the subject would indicate. The diagnosis, in Buerger's case, was not made during life. We should think of this possibility in cases of fracture associated with severe contusion and concussion. Patients of this kind should not be transported at once, but should be left absolutely quiet. An Esmarch should be placed above the crushed extremity for about one-half hour. In some cases Momburg's constriction at the waist line can be applied when the crushing injury is in the region of the pelvis. The object of this constriction is to encourage coagulation of blood in the region of the injured bone and thus prevent the fat from getting into the circulation. Buerger advises that the crushed wound be immediately opened and drained, or, if indicated, immediately amputated. But, of course, this is very difficult to do without some transportation. I get the same impression from reading Buerger's article on fat embolism, as in the study of the previous literature, namely, it is one of the risks one is compelled to take. We have no proof that we can recognize the complication in time to prevent it, nor any proof that it could be prevented when recognized.

One interested in that rare condition called *thymus death* will find an excellent article by Falls² from the Department of Experimental Medicine of the University of Illinois. He gives 53 references to the literature. My experience with the x-rays in the diagnosis of persisting thymus agrees with that of the Mayo Clinic—up to the present time it has not been helpful in a single case.

¹ Med. Klinik, 1915, xi, 996; review in Surgery, Gynecology and Obstetrics, 1916, xii, abstr. p. 194.

² Surgery, Gynecology and Obstetrics, 1916, xxii, 712, 746.

ANESTHESIA.

Space prevents an extended review. I have given my own impressions when discussing blood-pressure. The clinics which first began the routine employment of gas-oxygen anesthesia instead of ether are beginning to swing back to ether, but apparently the administration of ether is better than it was before the experience with gas. A number of my younger anesthetists who have been through this experience say their work with gas has made them appreciate the many factors which tend to safe operations and for this reason has taught them to give ether better than before.

I also get the impression that more surgeons are using local anesthesia, but it is still a small group.

Intratracheal Ether Anesthesia is being introduced in a number of clinics. Samuel Robinson¹ reports his experience with a new apparatus which he employs in his work in the Mayo Clinic and Major Allie W. Williams,² of the Army Medical Corps, has constructed a portable positive-pressure apparatus for the administration of ether by intratracheal insufflation. This has been tested at the hospital of the University of Pennsylvania and more recently in the field hospital in Texas. The apparatus will probably be a very important addition to the equipment of the automobile ambulance hospital, and all the mobile operating-room outfits which the present war conditions demand for the best treatment of wounds.

In my own practice, which has not included opening of the pleural cavities, I have not introduced intratracheal anesthesia. For all my operative work in the region of the oral cavity I prefer local anesthesia combined with ether, either given by the drop method or intrapharyngeally through a tube introduced through the nose. The anesthetic ether is never pushed to full narcosis. Years ago Kroenlein in his clinic succeeded in making a great contrast with the results of his colleagues in Germany in oral operations. He gave up deep narcosis and simply kept his patients slightly drunk with ether. This was before the days of local anesthesia. He reduced the postoperative mortality from something like 50 per cent. to less than 10. This application of partial general narcosis to oral surgery by Kroenlein was constantly dwelt upon by Halsted in the early years of the Johns Hopkins Clinic. In my more recent experience with cancer of the tongue, I have practically eliminated the mortality by the employment of local anesthesia in all cases, by using ether as a partial anesthetic when the operation could not be performed under local anesthesia alone, and by doing the operation in stages. The intrapharyngeal method puts the anesthetist out of

¹ Surgery, Gynecology and Obstetrics, 1915, xxi, 774.

² Journal of the American Medical Association, 1915, lxiv, 138.

the way as well as the intratracheal, eliminates all the difficulties of intubation, and requires very much less ether. I have tried the intratracheal method twice: It was given by an expert, but I could see no advantages, and I felt that it added to the risk of the operation.

Isabella C. Herb,¹ the special anesthetist to the Presbyterian Hospital in Chicago, gives a very clear description of the simplicity of the administration of ether. She is doubtful whether there is any advantage in warming ether vapors. The patient, however, should be kept warm. The ether should be diluted with as much air as possible.

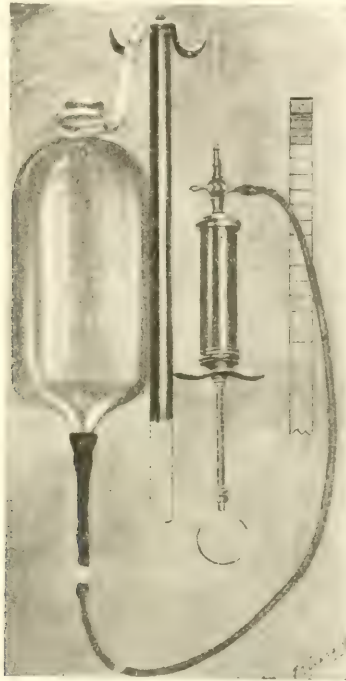


FIG. 39.—Showing container, syringe with two-way cock and infiltration needle; also centimeter measure. (Bartlett.)

Cooke,² of Los Angeles, speaking from the stand-point of a skilled anesthetist, states that local anesthesia is a most valuable adjunct to successful gas anesthesia, especially in abdominal work.

Carles and Charrier,³ from an experience with 200 operations in which *ethyl chloride* was the anesthetic, conclude that it is a much safer drug than chloroform and just as applicable to military surgery. They were able to compare these 200 operations with 500 in which the anesthetic

¹ Journal of the American Medical Association, 1916, lxvi, 1377.

² Ibid., lxvii, 175.

³ Review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 195.

was other than ethyl chloride. The patients are asleep in two minutes and wake up in a few minutes; the time of their operations varied from five to forty-five minutes; muscle relaxation is not as complete as under ether or chloroform. In France ether is apparently the anesthetic of choice in the base hospitals.

Willard Bartlett¹ has a very ingenious *continuous stream syringe apparatus* to help the tired surgeon with *infiltration anesthesia* (Fig. 39). I have tried all the new syringes, but always returned to the small, all-metal, hand syringe first advised by Braun. I will try Bartlett's arrangement. There is something, however, in the small hypodermic syringe which does not interfere with the surgeon's tactile sense, and when novocaine is used the nurse and other assistants have little else to do, so they can fill syringes. I am inclined to think the surgeon is apt to be wasteful with a larger syringe and, on account of the larger supply, infiltrate more than necessary.

Morian² found that 10 per cent. of his cases had albumin in the urine after local anesthesia with novocaine. It was observed in a few hours and usually disappeared in forty-eight. Microscopically, he usually found hyaline and granular casts, and sometimes red and white blood cells. All of the adult patients had morphine preceding the local anesthesia, and most of these patients suffered from vomiting after operation.

The presence of albumin in the urine after any operation is not at all unusual, and we have no evidence that this albuminuria indicates any permanent injury to the kidney. It could just as well be due to the absorption of sera or ferments from the wound as to the novocaine. We frequently see it after simple fracture without anesthesia. In my own experience, novocaine has been about as devoid of toxic symptoms as injections with simple salt solution.

ACCIDENT SURGERY.

American First-aid Conference. This new movement was described in detail in my³ last contribution. Since then the Board of Standardization has been appointed by the President of the United States, but has not yet made its report. First-aid committees have been appointed by all the national surgical associations and the majority of State medical societies.

The publicity given to the First-aid Conference and the educational work of the various committees has brought to the attention of the medical profession and the public the importance of this phase of

¹ Annals of Surgery, 1916, lxiii, 678.

² Zentralbl. f. Chir., 1915, xlii, 403; review in Surgery, Gynecology and Obstetrics, 1915, xxi, abstr. p. 547.

³ PROGRESSIVE MEDICINE, December, 1915, p. 217.

preventive medicine or public hygiene. But standardization of first-aid material and first-aid instructions is by no means accomplished.

Industrial Physicians and Surgeons. In my mind the most important advance in industrial medicine and surgery was the organization of the American Society of Industrial Physicians and Surgeons. The preliminary meeting took place in Detroit just before the meeting of the American Medical Association. Its members are chiefly physicians and surgeons in charge of the employees of great industrial plants and large department stores. It represents, then, the third national organization in relation to industry. The others are the different associations of railroad surgeons and the medical and surgical bureau of the department of mines. The problem of first aid and the treatment of accidental injuries are somewhat different in the three great industries.

When the employees are working in a single plant, it is possible to have in the plants first-aid material in boxes up to a fully equipped hospital. The first aid can be applied by educated foremen, trained nurses, or physicians and surgeons who spend their entire time in the plant. The development of the scheme is dependent upon the number of workmen employed and the number of accidents which cannot be prevented by all the precautions of "safety first."

The ideal arrangement, of course, is an operating room with modern equipment where physicians, surgeons and trained nurses are always present.

With such an arrangement, the interval of time between the onset of the injury or illness and the beginning of treatment is negligible. Transportation is a simple matter, and the first treatment is under the skilled hands of the educated physician and nurse.

I had the opportunity of inspecting the hospital which had just been opened in the Ford Motor Works in Detroit. There we find the dressing and operating rooms, the recovery room, and the constant attendance of surgeons and nurses. It is a miniature hospital. The movement, therefore, in industrial medicine and surgery is to shorten the time and the distance between the injured or ill laborer and the attending physicians and nurses, and the hospital itself. The same movement is taking place in military surgery. It is also expected to eliminate interference by all except those specially trained.

The ideal arrangement, of course, is only possible in the larger plant, and the probabilities are that the economic results in these plants will be such that ultimately some arrangement can be perfected by which all the employees will have the benefit of a hospital establishment.

If the number of employees is not sufficiently large to justify the establishment of a hospital within a plant, a number of smaller plants can be grouped around a hospital.

The problem is a little more difficult among miners and still more so on railroad lines, but there is no question that there is a wide-spread

movement having for its object the intensive study of the actual conditions of industrial accidents and the formation of a scheme of first treatment which will give the best results. There is yet much to be accomplished in this direction.

The relation between the medical and surgical departments of any industry and its employees is a far larger problem than the treatment of accidents, and undoubtedly the entire subject of the health and welfare of the workman will ultimately be placed in the care of trained physicians, surgeons and nurses.

First Aid. As stated in the beginning of this note, the Board of Standardization has not yet completed its work, but the Secretary of the American First-aid Conference has received about 500 replies to the five questions¹ and a large number of the first-aid committees have made an independent survey.

At the present time we may say that the consensus of opinion favors the immediate disinfection of the wound and its surroundings with iodine, and covering the wound with a piece of sterile gauze. If this treatment is not applied by an experienced surgeon, the patient should be transported as quickly as possible to the surgeon, or, in more serious cases, the surgeons brought to the patient. Now, this means that first-aid material will have to be distributed in convenient places throughout the industrial world. When there is a hospital in the plant, the problem is solved. In smaller plants the material is kept in a convenient cabinet, and the foremen are instructed in first-aid measures. In a little larger plant there is an accident room and an attending trained nurse. However, on railroads and in mines, the first-aid material has to be distributed in smaller quantities and the laborers themselves must receive the simplest instructions as to its application. There is apparently no difficulty in getting a good first-aid scheme on paper. The great obstacle is the instruction of single individuals in large numbers and the proper distribution of the packages in such a way that they will be available and not lost or wasted. Practically, all railroad and mining surgeons are giving these questions their attention, and on many railroads the first-aid arrangements are splendid and the good results are already evident.

When the injured, or ill, individual is not near a hospital, the question of transportation has to be considered. If there is a fracture, some fixation dressing will be required during transportation. For this reason laymen will have to be instructed in the simpler methods of fixation of fractures of the upper and lower extremity.

The majority of authorities are against instruction to laymen and women on the treatment of hemorrhage. In the first place, it is a rather difficult thing to tell whether the bleeding from a wound is copious

¹ PROGRESSIVE MEDICINE, December, 1915, p. 226.

enough to indicate an Esmarch bandage. Those who have had experience have found that when the untrained are given rules for the treatment of hemorrhage, the Esmarch is used entirely too often, and now and then with disastrous results. This also is the opinion among military surgeons. The injured had better take his chances with hemorrhage, unless a trained surgeon is present at the time of the injury.

Wound Treatment. Of course we find the same difference of opinion among industrial as among military surgeons in regard to antiseptics, in regard to the primary treatment of the wound, and as to the details of subsequent dressings. But they all agree as to the importance of the first dressing, and how essential it is to have this dressing done immediately after the wound is received. As I said in the beginning, iodine is first choice among the antiseptics.

The economic problem is an enormous one, and now the employer must pay the bill. Skilled treatment, therefore, means a shorter period of disability and the least amount of loss of function.

Preventive medicine and surgery will soon take their proper places in relation to the great industries. Proper book-keeping will show the economic value of modern medicine and surgery.

National Committee on Medical and Surgical Preparedness. This committee is the result of the movement in this country toward universal preparedness. The committee is composed of the presidents of the national medical and surgical associations and a few others. It has appointed subcommittees in each State. These committees are to act in consultation with the medical departments of the Army, Navy, and Public Health Service, and with the National Red Cross Association. A survey has already been made of graduates of medicine in every State whose fitness will make them available for the medical reserve corps. The national government, therefore, has had the benefit of the best representatives of the medical profession in obtaining the finest material for the reserve corps. The larger committee, working through the subcommittees, is making a survey of all the hospitals in the country, of surgical supplies and drugs. In this way the government will know exactly what is available and what needs to be provided for.

The larger committee, in conjunction with the National Red Cross, is establishing base hospitals in the larger cities throughout the country. Not only will the personnel of these hospitals be selected with the greatest care, but all the material necessary to equip a hospital of 500 beds will be purchased and stored ready for immediate use. A base hospital, therefore, will be like a fire department—organized, equipped, and ready to go on a moment's call when needed. Automobile hospital units and hospital trains are also being equipped.

The laboratory and experimental side of a hospital will be represented in every unit.

National Research Council. At the annual meeting of the National Academy of Sciences¹ in April, 1916, this National Research Council was appointed to offer its services to the President of the United States in the interest of national preparedness. The Academy seemed the proper agency to organize the scientific resources of educational and research institutions in the interest of national security and welfare. The President accepted this offer and representatives of the different government bureaus have been appointed to coöperate with the Research Council.

England has a somewhat similar scheme—a British Board of Science and Industry.²

The European War has undoubtedly fixed the attention of the medical profession on its weakness in coördination and national preparedness. These movements will tend to bring to all the people of the country what is best in modern medicine, surgery and science. The army today is better protected from infectious diseases than the people. Soldiers can get better medical and surgical attention. The people often have difficulty in selecting the best.

MILITARY SURGERY.

Organization. Hauser,³ writing from his observations with both the French and the German armies, is of the opinion that operating-room outfits should be brought closer to the firing line, as the experience of this war is clearly demonstrating that the more radical operative procedures, to be successful, should be done as quickly as possible after the injury and before a long transportation. Base hospitals' chief function should be for ward dressings and only for operations which admit of delay.

The French huge corps of stretcher-bearers grouped by divisions and capable of being distributed where needed most has proved most efficacious. The separation of the force in dressing stations and for transportation adds to efficiency. The smaller separate medical organizations for each French infantry regiment impresses Hauser as a much better plan than the German large medical staff for a whole division. I think this should be considered in the United States.

Hauser believes that the base hospitals should be small and widely scattered, and there should be numerous specialists' centers. That is, operations which can be postponed should not be indiscriminately sent to any base hospital, but the different types of operation should be sent to the surgeon or surgeons having at that time the largest experience in the treatment of the special condition.

¹ Science, 1916, xlv, 264.

² Ibid., p. 266.

³ Korrespondenzbl. f. Schw. Aerzte, November 13, 1915; review in Journal of the American Medical Association, 1916, lxvi, 153.

The smaller base hospitals, the convenient location for transportation, and the grouping of specialists is far more important than buildings or accommodations for large numbers of wounded. This is really the development of a small unit system.

First Aid on Firing Line. Spelman,¹ with the American Red Cross in Belgium, states that the emergency dressing consists in the application of tincture of iodine and sterile gauze, and the injection of antitetanus serum.

Mayo-Robson² favors the immediate employment of tincture of iodine in all wounds, and protection with sterile gauze.

Ferraton³ describes the little subterranean rooms used as first-aid stations in the French first line of trenches. A physician is stationed here who gives morphine for pain and injections of camphorated oil for shock. Here the wounds are examined, iodine and a dry dressing applied, fractures hastily and simply immobilized; now and then a bleeding artery is tied; at rare intervals tracheotomy is performed for threatening asphyxia. One can easily imagine that, if there were time for a little more digging, a larger and bomb-proof room could be provided, and an operating room, as suggested by Hauser and Fiolle, introduced.

Apparently, in digging the trenches, stretchers were not considered. As a rule, as Ferraton states, the soldiers must be transported on chairs or hammocks. It is quite possible that, in building a trench, provision for proper transport of the wounded could be made without increasing the work much, or taking away from the protective nature of the trench. We know that until recently, in building hospitals, little attention was paid to the transportation of the beds, even when splendid porches were erected.

Operating Room in Trenches. Under "Organization" we have just noted that Hauser favors an equipment for major operations nearer the firing line. Fiolle⁴ urgently advocates bomb-proof operating rooms in the trenches. The experience of this war has shown the enormous importance of immediate skilful surgical intervention.

Ferraton⁵ is of the opinion that the hospital with its operating room should be as near the firing line as possible. In his experience with the Fourteenth French Army Corps, he found that by employing special automobile ambulances for selected cases of wounded, these patients could be brought to the division hospital within from two to six hours.

¹ *Lancet Clinic*, 1916, cxv, 51; reviewed in *Surgery, Gynecology and Obstetrics*, 1916, xxii, 629.

² *British Medical Journal*, 1915, ii, 136; review in *Surgery, Gynecology and Obstetrics*, 1915, xxi, abstr. p. 630.

³ *Lyon Chir.*, 1915, xii, 565; review in *Surgery, Gynecology and Obstetrics*, 1916, xxii, abstr. p. 411.

⁴ *Rev. de Chir.*, February, 1916, No. 2; review in *Journal of the American Medical Association*, 1916, lxxvii, 81.

⁵ *Loc. cit.*

Transportation. Gros¹ objects to the war maxim of ammunition first, food second, and the wounded third. He also urges that the lines of transportation for troops and wounded should be the same. The solution of the problem are numerous automobile ambulances. The American Ambulance in Paris has demonstrated this.

Unit Plan for Base Hospital. The Medical Department of the Army has practically accepted Crile's² suggestion for the unit plan of organization of the Medical Reserve Corps for service in base hospitals. Colonel Kean, of the U. S. Army Medical Corps, has been assigned to the National Red Cross and is superintending the organization of these units and base hospitals. The suggestion comes from Crile, but the beginning of the scheme undoubtedly is due to the work of the units of the American Ambulance in Paris.

Gunshot Wounds. GENERAL. La Garde³ gives us a collective review on this subject in May, 1916. Colonel La Garde, M. C. U. S. A., is probably more familiar with the literature of military surgery than anyone else in this country. He has given us the best general book on gunshot wounds, and many of the reviews in the International Abstracts of Surgery are by him.

Therefore, it is interesting to see what he considers the more important contributions to, and the essential features in, the treatment of wounds in this war. He briefly describes the projectiles used at the present time and how the character of these projectiles influences the wound. The different bullets used by the French, English, Germans and Turks produce, as a rule, different types of wounds, while the shell wound is usually a pretty uniform one. In the latter there is always laceration and contusion of the tissue, and a great deal of hemorrhage into the cavity of the wound and its walls, while the character of the bullet wound varies from a simple, almost clean perforating track to a larger lacerated wound almost up to the extent of the shell wound.

It is in the lacerated, contused and hemorrhagic wounds that the infection finds its best medium, and the gas bacillus is probably present in all these wounds, although it does not manifest itself clinically in every case.

The characteristic features, therefore, of wounds in the present war are their size and the extreme degree of mechanical injury to the tissues, and the primary infection with gas bacilli.

La Garde expresses the opinion that the statement that first aid has failed in this war is due to the fact that too much was expected of it. It apparently has not failed in the simpler types of bullet wounds for which it was designed.

¹ Boston Medical and Surgical Journal, 1915, clxxiii, No. 1; review in Surgery, Gynecology and Obstetrics, 1915, xxi, abstr. p. 628.

² Surgery, Gynecology and Obstetrics, 1916, xxii, 68.

³ Ibid., xxii, abstr. p. 465.

A great difficulty in military surgery is the inability to control the environment. In many instances it is impossible to apply the treatment best at the appropriate time.

Then La Garde discusses the opposing methods of Watson Cheyne and Wright. The former is in favor of stronger antiseptics, the latter of salt solution only.

La Garde expresses the opinion that the majority of surgeons are in accord with the views of Wright, that it is impossible to disinfect with any antiseptic a huge lacerated wound primarily infected with foreign bodies and projectiles. La Garde makes no comment on the new antiseptic of Dakin, and, strange to say, he does not refer to Carrel's method of temporary drainage with secondary closure. Yet he has read about the method of primary excision of Milligan, discussed here.

Göbel¹ makes the following summary in his paper entitled "Mistakes in Military Surgery and How to Avoid Them."

The surgeon should change the dressings with sterile instruments, if possible, rather than the gloved hand, as it is easier to change an instrument accidentally coming in contact with something unclean, than a glove. Moist dressings should not be too wet. Remember that dressings applied as a circular bandage, constrict the limb when they dry out. Do not immobilize healthy joints if it can be avoided. Yet in a fracture of the femur, the healthy hip-joint, knee-joint and ankle-joint should be immobilized. Study the position in which joints are immobilized, selecting that position which will be best for function if ankylosis follows. Plaster casts should always be fenestrated over the wound. Extension weights are usually too light for fracture of the femur. Massage and passive motion to joints are usually neglected. Baths and hot-air apparatus are not employed as much as they should be. Consult the oral surgeon or dentist about all lesions in the region of the jaw.

Apparently, Göbel, as consultant surgeon to the German Army, witnessed all these mistakes or neglect. Yet he has not made a single statement with which every surgeon who treats wounds should not be familiar. Göbel is undoubtedly correct, but these are not mistakes especially confined to military surgery at the front. They are mistakes we see every day in civil hospitals. The fault, therefore, lies with the preliminary training of these men, suddenly called into military surgery.

When we come to *drugs* in the treatment of wounds, we find that this war has stimulated numerous surgeons to try different therapeutic agents. If they are good surgeons and know how to *d* ain, they all seem to obtain good results with almost any chemical agent. I have mentioned again and again that granulation tissue seems to do best on a changing and mixed treatment, providing certain fundamental things are not neglected. The fundamental things are: Frequent or continu-

¹ Review in Surgery, Gynecology and Obstetrics, 1915, xxi, abstr. p. 533.

ous irrigation with change of dressings, which can be accomplished in many ways; cleanliness; some form of antiseptic; proper drainage of deep cavities; comfortable dressings; methods to improve the general condition of the patient and to maintain good circulation in the region of the wound. Apparently, the two treatments which have made the greatest impression are Carrel's with Dakin's antiseptic solution, and Wright's lymph lavage. The drugs differ, but both methods depend upon continuous irrigation.

Other drugs mentioned are: A combination of iodine and sodium hypochlorite; quinine hydrochloride; epinephrin; magnesium chloride; silver nitrate; magnesium sulphate; urea; horse serum; salicylic acid; liquid paraffin with hypertonic salt solution; paraffin spray alone; Delbet's solution is anhydrous chloride of magnesium 12.1 parts to water 1000 parts.

Eusol, or hypochlorous acid, is recommended by Fraser and Bates¹ and does not differ in any material essentials from Dakin's fluid.

Among other treatments we have the early sterilization of the wound with hot air or oxygen; passive hyperemia; rest and moist heat; open air; filiform drainage; and Fonio's coagulen bandages for hemostasis.

WOUND TREATMENT. ANTISEPTICS. Matti² is of the opinion that physical and mechanical antiseptics are the chief therapeutic agents in wounds of war, but that at first chemical antiseptics are indispensable.

Hauser³ expresses the opinion that antiseptics are indispensable in military surgery.

Open Treatment of Wounds. Similar to Carrel's method of temporary drainage, this open treatment is not a new method, nor is it new in principle, but the demands for it have been forced upon the attention of surgeons of the world by the character of wounds in this war.

Schede⁴ is its principal advocate in Germany. When one has an open, granulating wound from which there is a profuse discharge, there must be some means for the removal of that discharge, irrespective of the condition of the wound. The continuous bath is one method, but this is not always applicable. The frequent dressing and irrigation is another method. This is pretty tiresome for both patient and attendant after a time. Schede would leave the wound uncovered and arrange for the secretion to drop into some receptacle. The wound can be cleansed whenever indicated, and the patient is not annoyed by a change of dressing. Figs. 40 and 41 illustrate schemes by which the extremity is immobilized, the wound left open, and provision made for the collection of the

¹ Edinburgh Medical Journal, 1916, xvi, 127; Surgery, Gynecology and Obstetrics, 1916, xxiii, abstr. p. 17.

² Review in Journal of the American Medical Association, 1916, lxvi, 388.

³ Loc. cit.

⁴ Deutsche Ztschr. f. Chir., 1915, cxxxiii, 617; review in Surgery, Gynecology and Obstetrics, 1915, xxi, abstr. p. 617.

discharge. Quite often exposure of the wound to sunlight and air decreases the discharge. The discharge from healthy granulation tissue is relatively insignificant. The discharge is increased by faulty circulation, dead tissue, and foreign bodies, and certain types of infection.

I will have to mention again and again, in the discussion of wound treatment, the remark of Matti that wounds do best when the treatment

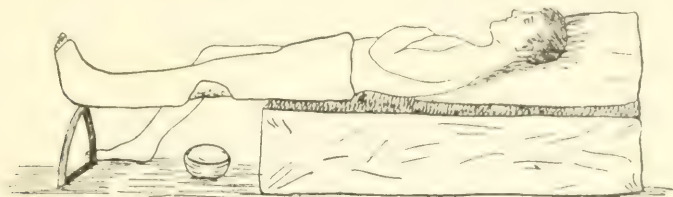


FIG. 40.—Arrangement for collecting discharge from a wound in open treatment of lower extremity. (Schede.)

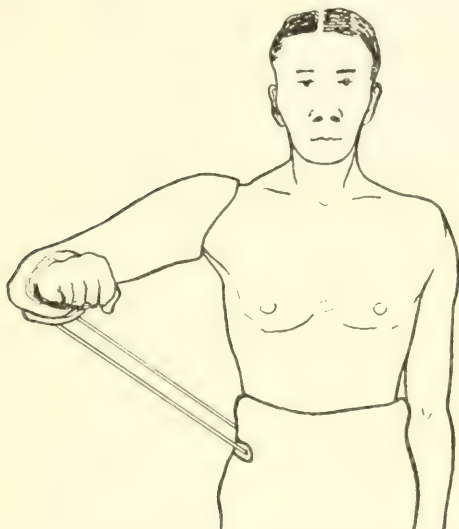


FIG. 41.—Arrangement for facilitating open treatment of wounds of upper extremity. (Schede.)

is changed from time to time, and the sage remark of Piper, of Philadelphia, that "war surgery is ward surgery." We know that a large amount of peace surgery is all done in the operating room.

In connection with Schede's open treatment, one should read in the original Bruns's¹ article on immobilization, leaving the wound exposed for any method of treatment, as shown in Fig. 42. In the December number of *PROGRESSIVE MEDICINE*, 1915, p. 293, through the

¹ *Deutsche Ztschr. f. Chir.*, 1915, cxxxiij, 593.

courtesy of Osgood, of Boston, I was able to reproduce illustrations of different types of fixation dressings which seemed to me to practically cover all the requirements. Dressings of this kind are conspicuous by their absence in the surgical wards of a general hospital, and I have the greatest difficulty in getting enough cases to teach my juniors these methods. One must have the skill of an orthopedic surgeon in the making of different types of fixation dressings, combined with a large experience in the treatment of infected and open wounds. This, with good judgment, is what is required most today in war surgery.



FIG. 42.—Arrangement for fixation extension and open treatment of wounds. (Bruns.)

Delbet¹ is of the opinion that the most powerful method of combating infection has been found to be the exposure of wounds to *air* and *sunlight*. After forty-eight hours of such exposures, pyocultures become negative. I believe Delbet is carrying this treatment a little too far. In the same article he finds that iodoform, ether, solutions of nitrate of silver, powdered lactose, or dioxygen, are of no value in rendering an infected wound surface free of bacteria. Yet, forty-eight hours' exposure to air and sunlight destroy them. One with any experience at all with infected wounds cannot accept such a statement. Undoubtedly, Delbet is attempting a careful bacteriological investigation, but he is falling into the errors of Schimmelbusch and many of his predecessors, of drawing conclusions from laboratory experiments and applying them to the human being. Unfortunately, this does not always work.

Dakin's Solution. Dakin's solution seems as popular with the French as lymph lavage is with a portion of the British medical service. Dakin² himself gives the following directions for the preparation of his solution:

¹ Bull. de l'Acad. de Méd., 1915, No. 23; review in Surgery, Gynecology and Obstetrics, abstr. p. 626.

² Presse Méd., 1915, xxiii, 377; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 74.

Sodium carbonate, anhydrous	150 gm.
or crystals	400 gm.
Water	10 liters

To this solution add:

Calcium chloride	200 gm.
----------------------------	---------

This mixture is shaken. In one-half hour syphon off the clear liquid and filter through cotton. To this filtered solution add:

Boric acid	40 gm.
----------------------	--------

Dakin is of the opinion that this solution is a strong antiseptic. The neutralization with boric acid renders the sodium hypochlorite less irritant.

It is a substitute, then, for antiseptics, such as carbolic acid, bichloride, iodine, and nitrate of silver. The principle, therefore, is antiseptic. But as it is, this non-irritating solution, which apparently has none of the dangerous poisoning qualities of carbolic acid, bichloride of mercury, etc., can be used in large quantities, and as a matter of fact, Dakin states, the best results are obtained by continuous irrigation.

He is also of the opinion that it aids in the dissolution of the necrotic tissue and has a slight hemostatic action.

Any solution used as a continuous irrigation must act mechanically and physically, so in Dakin's method we have, in addition to chemical antiseptics, this physical and mechanical factor.

Pozzi¹ gives Carrel's modification of Dakin's solution. (Apparently this was about March, 1916.)

Calcium chloride (chlorinated lime)	200 gm.
Ordinary water	5 liters

Mix in a 12-liter jar, agitate and allow to stand overnight. Then add

Sodium carbonate, anhydrous	100 gm.
Sodium bicarbonate	80 gm.
Cold water	5 liters

These are dissolved in the water before being added to the original solution. The mixed solutions are agitated for a minute, and then, after being quiet for one-half hour, the clear fluid is syphoned off and filtered.

These solutions must not be heated.

¹ Bull. de l'Acad. de Méd., March 21, 1916; review in Journal of the American Medical Association, 1916, lxvi, 1586.

Dakin's solution was discussed in the *Journal of the American Medical Association* of February 5, 1916, p. 447, and the Carrel method of employing it March 4, 1916, p. 775.

It will be observed that sodium bicarbonate has been substituted for boric acid, apparently the former is just as good for neutralization.

I referred to Dakin's solution under the title *The New Antiseptic* in my¹ last year's review. The note was based on an editorial in the *Journal of the American Medical Association*, September 4, 1915. In a later editorial² the editor refers to a more recent article of Dakin³ in which he disclaims any novelty in the so-called new antiseptic, and he quotes from his first papers that he made no claim for originality. If this solution proves to be as efficacious as the claims would indicate, Dakin deserves just as much credit as if he had discovered a new antiseptic, because this chlorinated lime, or Labarraque's solution, was not generally employed in the treatment of wounds, few surgeons knew anything about it, and still fewer had ever heard that Bertholet discovered this antiseptic in 1788. Nevertheless surgeons should have been thinking about these therapeutic agents. They had recently become prominent in public notice due to the chemical disinfection of city water at its source in the reservoirs and the disinfection of drinking water in the army. It is not exactly the same chemical substance, but in water the object was to kill the colon bacillus group, that is, the bacterium of the human feces, and apparently in wounds of war, and especially in trenches, these bacteria are largely responsible for infections. Dakin is of the opinion that the antiseptic action of hypochlorous acid is due to the formation of chloroimido, and not the liberation of oxygen. The direction for making the solution given by me at the beginning of this note are identical with that in an original article of Dakin.⁴

Carrel's Method. Apparently this attempt at abortive treatment of infection with early closure of large wounds is known in French and English literature as Carrel's method, but, as I brought out last year, the idea is by no means a new one and has occurred to many surgeons.

If possible, the first treatment should be within three hours after the injury. When introduced later, the chances of success are not so good. The wound is thoroughly washed out with Dakin's solution, foreign bodies are removed, dead tissue cut away, and the wound is closed with drainage tubes through which there may be further irrigation. These drainage tubes are removed when there are no signs of infection.

Carrel, Dakin and others⁵ give practically the above directions. If

¹ PROGRESSIVE MEDICINE, December, 1915, p. 269.

² Journal of the American Medical Association, 1916, lxvi, 430.

³ British Medical Journal, December 4, 1915, p. 809.

⁴ Ibid., 1915, ii, 318; review in Surgery, Gynecology and Obstetrics, 1915, xxii, abstr. p. 662.

⁵ Presse Méd., 1915, xxiii, 397; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 74.

Dakin's fluid is used as the irrigating fluid, it should not be heated, and alcohol should not be used in addition.

Tuffier¹ believes in the early disinfection of wounds and seems to prefer Dakin's solution. He uses a method for first treatment which is practically Carrel's. He describes his method somewhat as follows: Ether, if necessary, and not contra-indicated; cleanse the surrounding skin with iodine; irrigate the wound with Dakin's solution; make the necessary incisions for exploration, removal of foreign bodies and necrotic tissue; irrigate again; insert rubber tubes; pack cotton about the tube and bandage the wound loosely; the tubes project beyond the dressing; every hour Dakin's fluid is poured into the tube; the cotton dressing is changed but once a day.

Uffoltz² reports enthusiastically on the treatment of 18 cases in the environment of the field: 12 were extensive shell wounds, and 6 were bullet wounds. A large number of the cases were treated within three hours. All healed without any marked signs of infection.

G. Dehelly,³ a colleague of Carrel, summarizes the results of this treatment in 155 wounds on 48 men. The treatment was employed in 48 out of a total of 76 wounded. Of the 155 wounds, 135 were closed before granulation had begun, and 121 were closed before the twelfth day. There were about 22 fractures. The shortening of the average healing time is not the only advantage. There is less scar tissue and therefore less disturbance of function.

The exact technic of the continuous irrigation is given in a later number of the *Presse Médicale* by Dehelly and Dumas.

I believe it is better for one to turn to the original to get details of this kind. The reviews are thorough and accessible, and I cannot take space for the necessary details.

Personally, I cannot conceive that it makes very much difference—the wounds are irrigated, rubber tubes are left in the wound through which the wound is continuously irrigated, and the wounds are gradually brought together.

It is difficult for us to grasp a wound treatment of this kind at once. We are chiefly familiar with wounds closed and healing *per primam*, and wounds left open and healing by granulation. But this idea of Carrel is an old one; in the practice of peace it is, however, seldom employed. I remember distinctly assisting Dr. Halsted on several occasions when an abscess had been excised, or an infected joint resected, or an amputation for a grave infection performed. Fearing infection, these wounds were

¹ Bull. de l'Acad. de Méd., 1915, lxxiv, 314; review in *Surgery, Gynecology and Obstetrics*, 1916, xxii, abstr. p. 79.

² *Ibid.*, March 21, 1916; review in *Journal of the American Medical Association*, 1916, lxvi, 1585.

³ *Ibid.*, May 2, 1916; review in *Journal of the American Medical Association*, 1916, lxvi, 2042.

not closed at once, but the surfaces were kept apart by the introduction of rubber tissue; then the wounds were examined every day, and if there were no signs of infection, the rubber tissue was removed, the surfaces of the wound allowed to come together, and now and then a few sutures applied. Such wounds usually healed as if closed at the primary operation. We may speak of such drainage as temporary. I have employed this principle, which I have learned from Dr. Halsted, for now more than twenty years. The occasions to employ them have been rather infrequent. Carrel has shown the genius and ingenuity to grasp an old idea, or an old-established treatment of wounds, and apply it to military surgery. Apparently, the fear of infection had led to the wide opening of all these wounds, to keeping them open, and to the long, tedious period of healing from the bottom by granulation with its excess of scar tissue.

It is really a great triumph for a surgeon trained in the experimental laboratory to introduce such a practical change in wound treatment. If Carrel's method proves feasible, it will be a tremendous improvement, not only for the comfort of the wounded, but in ultimate efficiency, and it will be a great move toward economy. The average surgeon would fear to adopt such treatment. Forgotten methods are often considered unorthodox, but, from my limited experience, I know that it is an excellent method for temporary drainage. If the wound is too infected for closure, the patient has run no risk by this attempt: it takes but a moment to make it a wide-open wound to heal by granulation.

The method of continuous irrigation is not unlike that frequently employed after operations for empyema, or that developed by Young after perineal prostatectomy. The principle of the Murphy drip can be utilized. Bacteriological examinations can be made from the fluid coming from the wound and from these findings the decision as to when to close it can be made.

Even when these wounds do not heal *per primam*, there may be sinuses—one or more. But this complication interferes slightly with the result.

The last report from Carrel, Dehelly, and Dumas¹ was made some time in January, 1916, before the Paris Academy of Medicine. They have found that after temporary drainage and irrigation with Dakin's fluid, bacteria usually disappear from the wound, and the latter can be closed in from four to ten days. The wounds so closed heal just as well as wounds closed primarily. As a rule the apposition of the wounds is made by adhesive straps.

In the discussion Quénu and Bazy are of the opinion that the temporary drainage and continuous irrigation, and not the specific drug in Dakin's fluid, are responsible for the results.

¹ British Medical Journal, 1916, i, 211; review in Surgery, Gynecology and Obstetrics, 1916, xxiii, abstr. p. 65.

Moynihan,¹ who is one of the consulting surgeons to the British army in France, makes a report at about the same time as the above report of Carrel and his colleagues. He does not mention Carrel's treatment by name, but he reports that Dakin's solution has proved a very effective antiseptic, and does no harm to the tissues when employed as a continuous irrigant. The treatment recommended by Moynihan, except for the secondary closure, is practically identical with Carrel's.

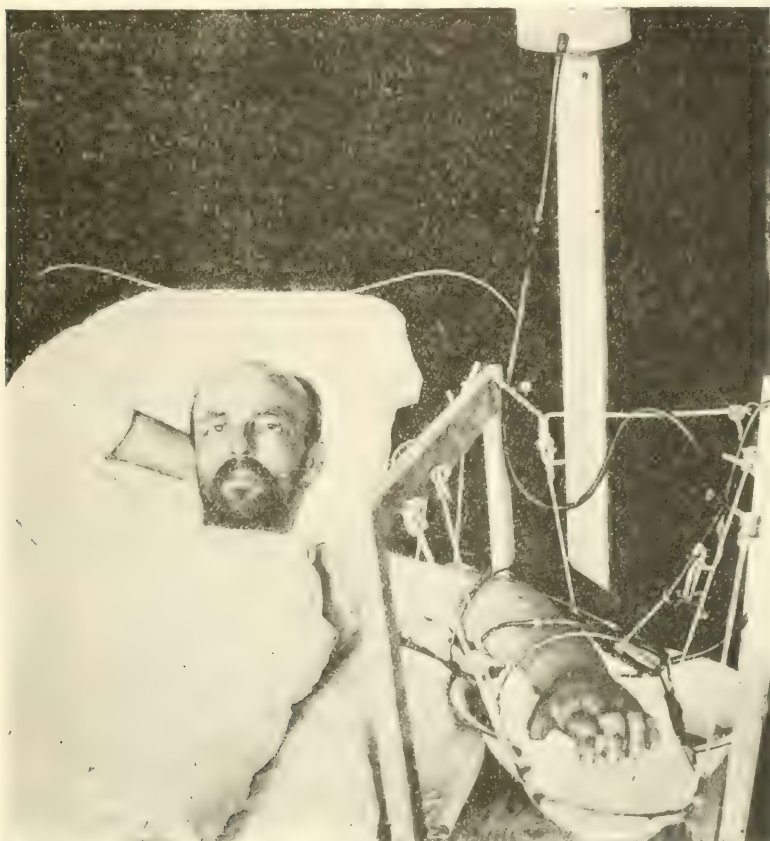


FIG. 43.—First case in which the described irrigation was used; multiple through-and-through wounds of the elbow. The result was satisfactory. (Piper.)

Irrigation. Edmund B. Piper² gives his experience with the University of Pennsylvania Unit at the American Ambulance in Paris in July, 1915. He emphasizes chiefly the importance of continuous irrigation of open and infected wounds, but states in italics: "No irrigation of any

¹ British Medical Journal, 1916, i, 333; review in Surgery, Gynecology and Obstetrics, 1916, xxiii, abstr. p. 65.

² Annals of Surgery, 1916, lxiii, 208.

type seems to be of any value unless there is proper and sufficient drainage." Again he writes: "War surgery is distinctly ward surgery." He means by this that the results of the treatment of wounds depend more upon the daily intelligent service in the wards rather than on what is done in the operating room, and the most valuable experience is the treatment of the wounds in the wards, and not operations in the operating room.

Various schemes were devised for irrigating the different types of wounds, as shown in Fig. 43.

The solution most frequently employed for irrigation and wet dressings were the sodium hypochlorite solutions (advocated by Carrel), normal salt solution, boric acid solution, and sterile water. The solutions were always hot, and, when used on gauze, the latter was well wrung out. Now and then alcohol and weak iodine were employed.

Of course there is nothing new in this method of treatment, but Piper has emphasized the importance of surgeons giving their special attention to the details of wound treatment in the wards. In time of peace the number of cases of this kind is small, and they are usually put under the care of the least-experienced interne.

This wound treatment can easily be directed by the surgeon. Nurses and orderlies take the greatest interest in performing themselves the necessary details of the dressings, and it is remarkable how quickly they become expert if they are only given proper directions.

Lymph Lavage. I presented this thoroughly and carefully last year,¹ based upon Wright's communication in the *Lancet* for April 24, 1915.

Chase² gives an excellent review of practically the same article, but published in the *British Medical Journal*, 1915, ii, 629, 670 and 715. As I wrote last year and still hold, Wright's lymph lavage is nothing more than the well-established bath treatment of wounds, continuous irrigation, or treatment with wet dressings. Wright, however, has been helpful by giving it a catchy name and adding a little mystery. The psychological effect of this has been that the overworked military surgeon will use Wright's lymph lavage with more enthusiasm than the same treatment under older names. It is the old method of getting an individual to take a bath by calling it a medicated bath and telling him to put salt in the water. Every report speaks of the importance of this wet treatment of wounds, especially in a stage of infection and suppuration, and before there is localization and the full development of granulation tissue.

SALT SACKS FOR DRAINAGE. Apparently wounds in war have stimulated research for newer methods. An English surgeon, A. J. Hull³ fills

¹ PROGRESSIVE MEDICINE, December, 1915, p. 264.

² Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 197.

³ *Lancet*, May 27, 1916; review in *Journal of the American Medical Association*, 1916, lxxvii, 79.

sacks made of bandages of four layers of gauze with salt. These salt bags of different sizes, very much like the Mikulicz pads for abdominal operative work, are sterilized dry in an autoclave and kept in stock sterile. Each sack has a tail representing the ends of the bandages making the sack. The wound, whatever its size, is filled with one or more of these salt sacks, and the tail coming out of the wound is placed in a receptacle containing saline solution, or tubes are introduced into the wound for drip irrigation. It is usually many days before the salt is entirely dissolved. Hull is of the opinion that this method of drainage is as effectual as if the wound surface was turned inside out.

EXCISION AND PRIMARY SUTURE OF WOUNDS. I have already referred¹ to Milligan's suggestion that the wound should be opened and the lacerated and contused tissue cut out. His article was published in June, 1915. Later, Gray² advocates this treatment in properly selected cases. Milligan objected to any antiseptic. Gray employs iodine in 10 per cent. solution. He does not drain. When this is possible, there is, of course, no question that it is the ideal treatment. It is my opinion that in this treatment suggested by Milligan and Gray there could be no objection to the disinfection with Dakin's solution, and to the temporary drainage in Carrel's method. If a wound would heal if sutured without drainage, nothing will be lost by the temporary drainage. I am also confident that surgeons with the best judgment who would follow the advice of Milligan and Gray would close some wounds that would have to be reopened later.

Moyrhan³ recommends excision of the wound when this is possible.

LOCATION OF THE FOREIGN BODY. Flint,⁴ of New Haven, presented this side of gunshot wounds before the American Surgical Association in May, 1915, well illustrated with lantern slides, and a number of these pictures appear with his paper. Fig. 44 gives an idea of the vibrating magnet of Bergonié. In the description of this localization there is a great deal of detail and a certain amount of mathematics. For this reason I must refer to the original, as it would require too much space for a review, to present the subject properly.

There have been other articles by Davidson,⁵ Herman-Johnson⁶ and von Hofmeister.⁷

¹ *PROGRESSIVE MEDICINE*, December, 1915, p. 266.

² *British Medical Journal*, 1915, ii, 317; review in *Surgery, Gynecology and Obstetrics*, 1915, xxi, abstr. p. 627.

³ *British Medical Journal*, March 4, 1916; review in *Journal of the American Medical Association*, 1916, lxvi, 1169.

⁴ *Annals of Surgery*, 1916, lxiv, 151.

⁵ *Lancet*, January 30, 1915; review in *Journal of the American Medical Association*, 1915, lxiv, 779.

⁶ *British Medical Journal*, 1914, ii, 752; review in *Surgery, Gynecology and Obstetrics*, 1915, xx, abstr. p. 173.

⁷ *Beitr. z. klin. Chir.*, 1915, xevi, 166; review in *Surgery, Gynecology and Obstetrics*, 1915, xxi, abstr. p. 58.

GRANULATING WOUNDS. Matti¹ confirms the experience of all older surgeons—that granulation tissue wounds do best when the treatment is frequently changed; not only the type of the treatment, but the drug. My own experience confirms this too. Frequent irrigation with hot water stands first, but other things are helpful in turns and under proper supervision: Alcohol, ether, balsam of Peru, castor oil and bismuth, boric acid-vaseline. When there is excessive secretion I agree with Matti that exposure to the sun and air are very beneficial.

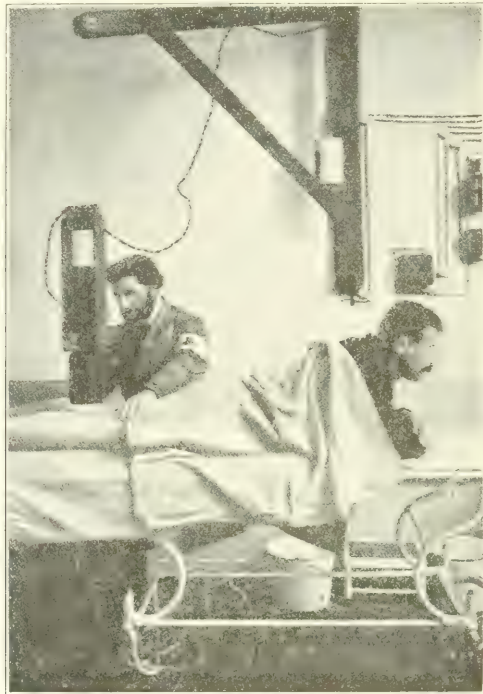


FIG. 44.—The vibrating magnet of Bergonié.

SECONDARY HEMORRHAGE. One is surprised at the absence of literature on this subject, and in all the descriptions which I have been reading recently of wounds in war I find little, or no, reference to this complication. If this means that secondary hemorrhage is not a frequent complication, we may be quite certain there has been a great improvement in the treatment of infected granulating wounds. I find but one reference to secondary hemorrhage by Morris.² He reports five cases in detail. I have referred to the coagulen bandages of Fonio, and there

¹ Loc. cit.

² Military Surgeon, 1916, xxviii, 131.

is a recent article by Cronin¹ on thromboplastin, a tissue extract to be used as a hemostatic.

WOUNDS OF HAND. Witzel² is interested in the great industrial importance of preserving the function of the hand. It is not so much the actual wound which impairs later function, but phlegmon. This should be borne in mind at the first and subsequent dressings. Recent wounds of the hand should never be closed, often they should be enlarged. One or more cuts on a hand will never impair function. For the first few days hand wounds should be seen frequently, and the dressings changed; never employ a tight dressing. Witzel favors Bier's hyperemia to prevent infection.

In my own personal observation I can get along without Bier's hyperemia if I can see the patient first and provide for frequent dressings. In the second stage, passive motion and massage to maintain function must not be neglected. Then, in more severe cases, special treatment, such as elastic traction of the fingers, aid in restoring function.

Gunshot Wounds of Joints.—**FIRST TREATMENT.** Varay³ advises immediate fixation of the injured joint. Arthrotomy should not be performed at once, even if diagnostic aspiration demonstrates the presence of bacteria in cover-slips and culture. Arthrotomy is not indicated on the bacteriology of the joint effusion, but on the clinical symptoms. On the slightest clinical signs there should be arthrotomy and drainage, and the most effective arthrotomy is one early after the injury. The incision should be free to allow full inspection of the joint. When the local conditions are serious, resect at once. This is, however, rarely indicated and still more infrequently amputation. However, the surgeon is fortunate who has the experience and judgment to recognize those cases which require primary resection or amputation. Varay expresses it very well, when he writes that the operation should precede, and not follow, the course of the infection.

Roux⁴ is inclined to think that primary resection affords better drainage and shortened convalescence. If there is much destruction of the joint, the chances after arthrotomy and drainage are that ankylosis will take place. In wounds in the present war, conservative treatment has done harm, and when the conservative surgeon becomes radical, he is too late.

I⁵ went into this subject thoroughly in 1900 and since then I have paid special attention to the literature and to the few cases which have come

¹ Journal of the American Medical Association, 1916, lxvi, 557.

² Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 389.

³ Lyon Chir., 1915, xli, 654; review in Surgery, Gynecology and Obstetrics, 1916, xxii, 499.

⁴ Deutsche med. Wehnschr., 1915, xli, 1474; review in Surg., Gynec. and Obstet., 1916, xxii, 500.

⁵ PROGRESSIVE MEDICINE, December, 1900, p. 170.

under my observation. Joint infections in peace practice are relatively infrequent. I agree entirely with Halsted, however, as to the importance of early arthrotomy, and also as to the danger of introducing drainage of any kind into the joint cavity between the cartilages—simply leave the wound open and irrigate it continuously or at frequent intervals. I have always been of the opinion that when a joint aspiration shows the presence of organisms, nothing is to be gained by putting off arthrotomy, and am confident that if we follow Varay's advice and base our indication of arthrotomy on the clinical signs only, we will open unnecessarily a number of joints and delay treatment in some badly infected joints. Again and again have I seen locally a marked arthritis with temperature and leukocytosis which has recovered without arthrotomy, which was not performed because the aspirated fluid was sterile. Then again, in a case clinically less severe, we have found organisms on aspiration. These cases have been reported in detail in previous numbers of *PROGRESSIVE MEDICINE*. Varay's description of his two cases rather impresses me as proof of the correctness of my attitude. In the most severely infected case the local symptoms were least, and for this reason arthrotomy was delayed. Had aspiration been performed, twenty hours might have been saved.

Zahradnicky¹ reports on his experience with 200 cases of gunshot injuries of large joints.

Infection took place in only 67, about one-third of the cases. There were four deaths from sepsis (2 per cent.)—one hip and three knee cases. Restoration to function took place in about 80 per cent. of the non-infected joints, and 18 per cent. of the infected joints. However, it is only fair to say, these are rather immediate results and represent the worst. Later orthopedic treatment will improve many. He advises puncture to remove blood and fluid, fixation with compression; in some cases after aspiration the joint may be irrigated with a 1 per cent. carbolic solution. If conservative measures fail to relieve the clinical signs, there should follow free arthrotomy and drainage; if this, too, fails—resection.

The author operated on about 28 per cent. of all his cases, while in the hands of colleagues operations varied from 4 to 95 per cent.

In my own experience with joint surgery, I am confident that if operations can be performed under the proper environment, no harm will be done, and I thoroughly agree with Varay in the danger of delay. It requires a very large experience and well-developed judgment to be successful in selecting the cases in which operation is indicated. Therefore, for the surgeon who has less experience, but good technic and skill, it will be safer to always ascertain by aspiration the bacteriology of the

¹ Beitr. z. klin. Chir., 1915, xcvi, 452; review in *Surgery, Gynecology and Obstetrics*, 1916, xxii, abstr. p. 289.

joint, and by x-ray the actual conditions of the bones and the position of the bullet, and, if still in doubt, to open and irrigate. When the local conditions are such that he can be quite certain that ankylosis will result, it is best to perform a typical resection, the type varying with the different joints. As has been stated before, this provides for better drainage. Why, therefore, increase the risks of infection, when there is no chance of restoring joint function.

Auvray¹ is of the opinion that by early resection he saved limbs and lives. Kirmisson, in the discussion of his paper, differed. This, of course, is still the same controversy that has gone on for years, and may be explained by the fact that the surgeons are talking about different types of cases. Lockwood² lays especial stress on the early removal of foreign bodies and loose bones. This, of course, is a typical resection; in the second place, he recommends perfect immobilization; in the third, the lapse of at least three weeks before beginning passive motion.

Hansing³ confines his investigation to the knee-joint. He had 34 cases, 23 of these infected. He uses exploratory puncture for diagnosis, then rest and Bier's hyperemia; then multiple incisions with free drainage. When bacteriological examinations show streptococci, he is inclined to amputate, especially if the joint wound is complicated with fracture into the joint. Apparently, Hansing had to amputate more than others. It is possible he had late cases.

I get the impression from Hansing's remarks that he pushed conservative treatment in infected knees too long and agree with Fresson⁴ as to the importance of early intervention in knee-joint infection, but I do not like his gauze drains. In the discussion of his paper, Chevassu is convinced that the interval of time between the wound and the arthrotomy has more to do with the result than any other factor.

BACTERIOLOGICAL CONTROL. R. Gaultier⁵ follows Carrel's method of wound treatment and checks every case with bacteriological examinations. This confirms the statement that I have made as to the importance of knowing the bacteriology of the infected joint before deciding as to treatment.

HYPEREMIA. I do not know how much Bier's hyperemia helps when the joint is really infected, especially in gunshot wounds, but, it is very important in the after-treatment. Yet, Linberger,⁶ who never before

¹ Journal of the American Medical Association, 1916, lxvi, 1715.

² British Medical Journal, January 29, 1916; review in Journal of the American Medical Association, 1916, lxvi, 773.

³ Beitr. z. klin. Chir., 1915, xevii, 32; review in Surgery, Gynecology and Obstetrics, 1915, xxi, abstr. p. 626.

⁴ Journal of the American Medical Association, 1915, lxv, 1658.

⁵ Paris Méd., 1916, vi, 43; review in Journal of the American Medical Association, 1916, lxvii, 642.

⁶ München. med. Wehnschr., February 29, 1916; review in Journal of the American Medical Association, 1916, lxvi, 1359.

approved of Bier's hyperemia, now speaks of it enthusiastically. He was induced to renew his trials with this method by the favorable reports of Sehrt.¹

Cotton² is apparently referring to joint infections of a different character from those in gunshot wounds. He depends upon irrigation of the joint for fifteen minutes with 1 to 15,000 solution of bichloride of mercury followed by salt solution. Then he closes the synovial membrane and leaves the external wound open. This is the treatment first advocated by Halsted over twenty-five years ago, and which I discussed fully in the December number of *PROGRESSIVE MEDICINE* in 1902. The best results are in gonococcus cases. In infections with strepto- and staphylococci Dr. Halsted was inclined to leave the entire wound open for repeated irrigations should these become necessary. The chief point Halsted made in this treatment was that gauze drainage was harmful in joint wounds.

I have been over this subject continuously for a quarter of a century, and I am confident that surgeons should give more attention to Halsted's views in joint infections. To open and wash out a joint under proper precautions never does any harm. If performed early, it generally accomplishes a result at once. If the wound is left open and the disinfection has been successful, the wound will heal almost as quickly as when sutured. If this disinfection has not been sufficient to destroy the organism, the open wound prevents retention of infected synovial secretion and gives an opportunity for continuous or repeated irrigations. I have a large experience with cases of the kind described by Cotton, but when we have a gunshot wound associated with a foreign body in the joint and fractures communicating with the joint, the problem is a much more difficult one. In 1899³ I reported a bullet wound of the knee-joint. Twenty hours after the injury I expressed gas and serum from the external wound, and found in the cover-slips cocci and a large bacillus. Within one hour Dr. Halsted performed arthrotomy, removed the bullet imbedded in the tibia, irrigated the joint with 1 to 1000 bichloride of mercury, but closed the wound. It was our first experience with an infected bullet wound of the knee-joint, and it was the first gas-bacillus case (March, 1895). Previous to this time we had been very successful with such irrigations and had often closed the external wound. From the joint secretion in this case, Dr. Welch cultivated the gas bacillus and the streptococcus. Forty-eight hours later the joint was reopened and irrigated, but seven days later it was necessary to amputate. One naturally asks the question, what would have been the result if this wound had been left open?

¹ München. med. Wehnschr., 1916, lxii, No. 10; review in Journal of the American Medical Association, 1916, lxvi, 1359.

² Boston Medical and Surgical Journal, 1915, clxxiii, 905.

³ *PROGRESSIVE MEDICINE*, December, 1899, p. 159.

I would strongly advise surgeons never to use the treatment advised by Cotton in infected joints associated with an external wound of any character, and I am inclined to think that it is safer in all cases, except gonorrheal infections, to err on the side of leaving the joint open, but I agree with Halsted that drainage into the synovial sac, especially with gauze, does not help the joint to take care of the infection.

RESECTION. One familiar with the older literature on resection of joints will find nothing new in the literature of the present war in regard to resection for infected joints secondary to gunshot wounds. The problems of resection have been solved long ago. In an infected gunshot wound, the chief question is as to the indications for resection, and when resection should be done. To a certain extent I have already covered the ground.

Resection of joints for tuberculosis has in recent years been a rare operation, so that the younger surgeons had very little experience to help them when confronted with this problem. We know that a resected joint will take care of an infection better than one with cartilage covering the bones and with its many recesses difficult to drain. Apparently, one must resort to resection most promptly for infections of the shoulder and hip. In the shoulder, function after resection is very good, and, as a rule, in the hip we can accomplish strength with some motion. One always attempts to save the knee-joint longer than any other, because resection here means ankylosis. With the elbow, wrist and ankle, the functional results are very good, but, as with everything else, in surgery we cannot depend much upon statistics when the intervention has been a late and last resort. The failure is not due to the method, but to the surgeon, and, of course, the problems in infected gunshot wounds of the joints are much more difficult than in tuberculosis.

Burekhardt and Landois,¹ in their two papers go over the entire subject. In infected hip-joints, resection rarely saved the life of the patients. After resection of the knee-joint, there was a large percentage of pseudarthroses. In the other joints the results were excellent.

POSITION FOR ANKYLOSED JOINTS. One must always bear in mind, in a gunshot wound involving a joint, that in spite of treatment, ankylosis may be the end-result. For this reason the position of the extremity deserves special attention. Robert Jones,² of Liverpool, gives the following rules: The arm should be abducted fifty degrees; the elbow should be slightly in front of the coronal plane of the body, so that when it is at a right angle and the forearm supinated, the palm of the hand is toward the face. As for the elbow-joint, by far the greater number of

¹ Beitr. z. klin. Chir., 1916, xcvi, 358; review in Surgery, Gynecology and Obstetrics, 1916, xxiii, abstr. p. 42, and München. med. Wehnschr., 1915, No. 21; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 609.

² British Medical Journal, April 29, 1916; review in Journal of the American Medical Association, 1916, lxvi, 1823.

men would prefer the fixation to be just below a right angle, that is, about one hundred degrees. If both elbows are to be ankylosed, fix one at eighty and the other at one hundred degrees. If pronation and supination are to be lost, try to fix the forearm in mid-position. Hold the wrist in dorsal flexion; keep the hip in slight abduction; the knee fully extended; the ankle with foot at right angle. Overcorrect in wounds of the tarsus and metatarsus to prevent, if possible, flat-foot.

Of course these are old rules which had naturally been forgotten because this type of wound and surgery was becoming rare in modern times. When one has a severe infection of the joint and is attempting to save, first, joint-function, and then the limb, no matter what becomes of the joint, it is very difficult to maintain these positions, and unless they are the best positions for the treatment at that time, no attention should be paid to them. First think of saving joint-function, if possible; if this becomes hopeless, concentrate your attention on saving the limb. If you accomplish this, there will always be opportunity for later correction of the position of the ankylosed joint. Nevertheless, Jones calls attention to a point in treatment usually overlooked, and in my experience we can as a rule give attention to this point and keep the limb in the best position. We must also remember that an ankylosed ankle or elbow, or wrist, may give a much more serviceable arm than pseudarthrosis. The chief danger of resection is weakness and flail-joint.

One should never resort to resection during the septic stage of the wound, except for the purpose of saving the limb, because experience has shown that joint-function may be restored after the severest infection and gravest injury. It may require a year or more of hard work on the part of the patient, and coöperative help with mechanotherapy.

Gunshot Fractures. Fractures in war are generally compound, usually infected. In the first instance, the wound demands the closest attention, then some fixation dressing which will hold the bone in as good a position as possible while the wound is healing; then comes the stage of non-union, faulty union, chronic osteomyelitis, ankylosis of joints, tendon fixation, and nerve injuries. From the very onset, therefore, of a gunshot fracture there are many orthopedic problems.

MILITARY ORTHOPEDICS. The British War Office has appointed Robert Jones¹ Inspector of Military Orthopedics. Special hospitals have been provided and more will be developed for the treatment of these cases. Here will be assembled the end-results of wounds of the extremities and perhaps of the spine, to see what orthopedics can do to relieve the handicap. Here also attention will be devoted to amputation stumps which require the supervision of a specialist for the measurement and adjustment of artificial limbs. It is reported that cases of this kind are being admitted at the rate of 300 a month. Other types of

¹ *Journal of the American Medical Association*, 1916, lxvi, 1716.

cases are chronic joint lesions, badly united and ununited fractures, loss of function due to injury of muscles, ligaments or tendons; nerve injuries, stiff joints. These hospitals will not only be specially equipped with orthopedic surgeons, but with all the apparatus and trained staff for all the forms of mechanotherapy.

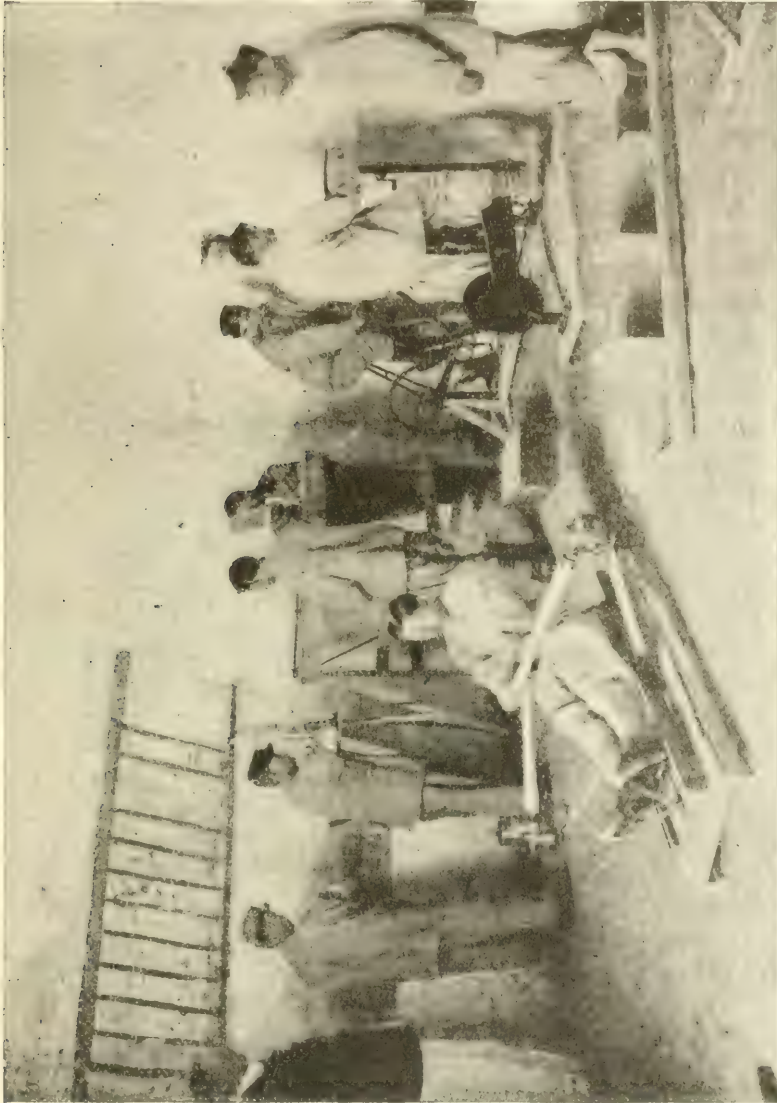


FIG. 45.—View of the mechanotherapy room. (Flint.)

Flint¹ gives us the best description of the means adopted to expedite these. In reproducing his Fig. 2 (Fig. 45) I may omit any further description of the different types of apparatus.

¹ Surgery, Gynecology and Obstetrics, 1916, xxiii, 228.

I would suggest to all surgeons connected with railroads, mines, and other industrial plants, to read this article of Flint, especially if they have provided no means for the proper after-treatment of the wounds they are called upon to treat.

Lange¹ covers a much larger field. He begins with first aid. He states that physicians on the firing line need orthopedic training; field ambulances and moving hospitals should be properly supplied with plaster-of-Paris bandages. Lange apparently believes that this fixation dressing is the best, even immediately after the injury. He also advises a special hammock for the transportation of this type of wounded when they are carried in auto-trucks. On trains he advises the use of stretchers. These patients should be taken to special hospitals.

The majority of authorities seem to be against the use of plaster of Paris as a first dressing and for transportation. It would complicate matters to have so many types of stretchers. Cushing has pointed out that it is very convenient to have a uniform stretcher for all cases.

A surgeon trained in the use of orthopedic apparatus should be part of every medical unit.

Greenough, Osgood and Vincent² give their experience with the treatment of 129 compound fractures in the service of the Harvard Unit at the American Ambulance in Paris. These cases came under the care of the authors on an average three days after the injury. The wound in every instance had been treated with iodine, tetanus antitoxin had been administered, and the limb had been immobilized in tin or aluminum splints. Three out of 121 compound fractures healed by first intention. Their conclusions are as follows:

In the first instance; anesthesia, enlargement of the wound, removal of foreign bodies, cleansing, drainage. Then complete immobilization in extension with plaster put on under anesthesia; provision in the plaster dressing for frequent and painstaking dressings of the wound; immediate attention to those details which will prevent ankylosis of joints and correction of contraction of tendons and muscles.

Through the courtesy of Osgood, I was able to reproduce in *PROGRESSIVE MEDICINE* for December, 1915, p. 292, a large number of photographs illustrating the different fixation dressings employed by Osgood and his colleagues during their sojourn with the American Ambulance. I am quite sure these pictures will become classical as illustrating the proper methods and refinements in the art of fixation of fractures when there is an open and infected wound.

X-RAYS. Major Clyde S. Ford has given us one of the most comprehensive series of 162 röntgenograms of gunshot fractures collected in the hospitals of Constantinople during the Balkan wars. These 162 plates

¹ *Ztschr. f. orth. Chir.*, 1915, xxxv, 3; review in *Surgery, Gynecology and Obstetrics*, 1916, xxii, abstr. p. 609.

² *Boston Medical and Surgical Journal*, 1916, clxxiv, 37.

were selected from 1500. The book is Bulletin No. 9, October, 1915, War Department, Office of the Surgeon-General. Anyone interested will have no difficulty in obtaining a copy on request. With each plate there is an excellent clinical note giving the details of the case.

OPERATIVE TREATMENT. Last year I covered the ground pretty thoroughly in regard to the treatment of gunshot fractures, and called attention to the fact that the majority of surgeons objected to any method of plating in the early stage of wounds.

Lake,¹ a British surgeon, gives his nine months' experience in the military hospitals in France. During this time he did not see any plating of gunshot fracture. However, he seems to be of the opinion that this plating might be done earlier.

Lanc² states that, with few exceptions, it is advisable to postpone plating until the wounds have healed.

I have been most impressed, from personal conversation and from the study of the literature, with the wonderful results in bone healing in gunshot injuries when the position of the fragments has been maintained by proper fixation dressing or extension. In a gunshot fracture there is usually comminution. It is less difficult to maintain position than in cases in which we have only two fragments, and, as a rule, uninjured tense muscle. The greater the comminution, the more callus, if the infection is not too intense. From this, I am impressed that plating and other methods of bone fixation will rarely be necessary, except in a small group of cases in which the results obtained are not satisfactory, either because of non-union or faulty union. When we go over the special reports of different fractures, it would seem that the results obtained in the healing of the bone lesion are as good as, or even better than, the results of the treatment of simple fractures in time of peace. We must also bear in mind that the gunshot fractures are absorbing the attention of the best minds in the military hospitals of all countries. It is the chief work of the military surgeon, while in peace times fractures are not usually under the care of the most experienced surgeons, and the younger group of surgeons has had poor instruction.

John B. Roberts³ is of the opinion that the treatment of fractures is a lost art. I might agree with him if he considers only the evidence accessible in this country. In the hospitals at the fronts today, he will find a renaissance in the art of treatment of fractures.

¹ British Medical Journal, 1915, ii, 44; review in Surgery, Gynecology and Obstetrics, 1915, xxi, 527.

² Practitioner, March, 1916, xevi, No. 3; review in Journal of the American Medical Association, 1916, lxxvi, 1170.

³ Pennsylvania Medical Journal, 1915, xix, 74.

INFECTION.

Surgical Bacteriology. In my paper before the American Surgical Association,¹ in May, I wrote: "The successful development of aseptic surgery has apparently influenced surgeons and bacteriologists to discontinue their interest in, and investigations of, bacteriological problems."

This explains why we were not prepared for the avalanche of infected wounds in this war.

The great success of the preventive treatment of tetanus and typhoid fever clearly shows what would have been the different conditions of these wounds had there been a more intensive investigation in the surgical bacteriology of infected wounds. Welch and Nuttall discovered the gas bacillus in 1892, but little or no investigation was attempted for the discovery of a preventive or curative serum or a chemotherapeutic agent.

The surgery of infected wounds was thoroughly developed before the days of Lister, and, up until about 1895, in the majority of hospitals there was a sufficient number of infected wounds, accidental and operative, to keep up the interest of the surgeon and furnish him with material for teaching.

Personally, I have seen very few infected wounds since 1900. Surgeons whose medical education began at this time apparently know very little about these well-established older procedures.

These two factors explain the feeling of helplessness among the younger modern surgeons when they were confronted with the terrible wound infections in France.

This war has stimulated tremendous interest in the bacteriology of wounds and in laboratory investigations having for their object the discovery of some curative serum or chemotherapy. The literature is too voluminous to be discussed here. Duncan, Gardner and Bawtree² give a very good resumé of their investigation of the bacteriology of shell wounds. I must mention also the splendid work of Weinberg on the gas bacillus. Fleming³ investigated chiefly infected wounds. He divided the demonstrable organisms into three groups: (1) Spore-bearing microbes of fecal origin; (2) non-spore-bearing microbes of fecal origin; (3) pyogenic cocci.

In the first group we have the tetanus and gas bacillus, and some putrefactive bacilli, called by Fleming *X* and *Y*. In the second group, he places the proteus, colon, whip bacillus, and, most frequent of all, the

¹ *Surgery, Gynecology and Obstetrics*, 1916, xxiii, 182.

² *Lancet*, June 12, 1915; review in *Journal of the American Medical Association*, 1915, lxxv, 200.

³ *Lancet*, September 18, 1915; review in *Journal of the American Medical Association*, 1915, lxxv, 1491.

streptococcus. That is, Fleming is of the opinion that the streptococci also come from the intestine. Of the third group, the pus-producers, the most common is the *Staphylococcus aureus*. The probabilities are that this organism comes from the skin of the individuals.

As a rule it is the streptococcus when the blood cultures are positive.

Fleming is also in favor of autogenous vaccines, as he is of the opinion that it will aid and maintain the resistance of the patient. Every case should receive a streptococcus vaccine in small doses, one to five millions every five or six days.

In brief, the bacteriology of the wounds in this war has discovered no new organism, nor has there developed any new type of wound infection. The presence of any or all of these bacteria has been found in many wounds in which there was no local evidence of a grave infection—the gas bacillus without gas; streptococci without lymphangitis; the bacillus of tetanus without lockjaw. This, of course, is not a new observation, but an indication that surgical bacteriology and the demonstration of the different forms of organisms in the wounds of surgical infections or of their absence has reached the limit of discoverable possibilities. However, further investigations along the line of surgical bacteriology, with the hope of discovering a curative serum or some chemotherapeutic agent, were by no means exhausted. If this war will lead to such discoveries, great good will have been accomplished.

Foreign Bodies. Walton Martin¹ draws a sharp contrast between what we know of foreign bodies introduced into the tissues with the least possible trauma and with as little infection as possible, and the foreign bodies introduced with enormous trauma and very much infection.

This undoubtedly explains the frequency of infected shell wounds in the present war. Martin's contribution with its twenty-seven references to the literature on this subject may be looked upon as the most recent and thorough article on foreign bodies in the tissues. From my own reading and investigations, I am inclined to the view that injured tissue and infection play the larger part, and perhaps, of all, it is infection which is chiefly responsible for the results. In a comminuted fracture we have foreign bodies in the loose fragments, and the contused tissue may have as poor a circulation as an open shell wound, and there is also a hematoma. But if the skin is unbroken and the patient has no focus of infection to disseminate bacteria throughout the circulation, this subcutaneous wound heals without suppuration or other signs of infection. We are informed that shell wounds received on shipboard differ very little in character from those in the trenches. Infection, however, is rare in the former and the rule in the latter. It is readily conceivable, therefore, that if we could supply the human organism with something that would destroy the bacteria we would have no difficulty in accomplishing

¹ *Annals of Surgery*, 1916, lxiii, 24.

the perfect healing of the wound in spite of foreign bodies, or dead tissue, provided there is enough circulation to prevent gangrene.

Pyoculture. I had some difficulty in finding out exactly what this meant. It is first mentioned in the *Journal of the American Medical Association*, June, 1915, lxy, 183. In a letter from Paris to the *Journal of the American Medical Association*, Pierre Delbet, a surgeon, is said to take cultures from the pus in bouillon and to place in similar tubes, without bouillon, the same pus. Then he compares the growth of bacteria in each. If the growth in the pus is greater than in the bouillon, operation is indicated, and the prognosis is bad, but if there are a few, or no, organisms in the pus, it is a sign that the patient has good resistance. Delbet is of the opinion that this pyoculture test is a better index to the actual condition of the patient than Wright's opsonic index. Delbet has also used this method to test different forms of wound treatment, and from his investigations he concludes that antiseptics are useless and some are harmful. He therefore favors asepsis, and all solutions should have the molecular concentration of the blood serum. In addition, he is a great believer in the exposure of wounds to air and light, claiming that by this treatment a positive pyoculture may become negative in forty-eight hours. Carrel also, in his treatment of wounds, uses a bacteriological test.

Barnsby and Truffier¹ describe a case in which pyoculture tests prevented them from reopening an infected knee. The patient recovered with good function. In a second case, pyoculture led them to amputate the thigh for infected knee.

Surgeons familiar with infected wounds, have listened to this patiently before in regard to the opsonic index and vaccine treatment, and they should listen to Delbet's pyoculture. But when, in their own experience, they have had a much larger number of cases corresponding exactly to those reported as proving the truth, they naturally must be skeptical. For example, we have no evidence that pyoculture was correct in indicating to Barnsby and Truffier that the limb should be amputated for the infected knee. It is quite possible this patient might have recovered without amputation, and in his first case we know there is always a local reaction after opening and irrigating an infected knee-joint. As compared, therefore, with my own experience, I am unable to see anything in the pyoculture test. I am convinced that we should know, if possible, whether organisms are present or not, and their character. This is especially true in joint infection. I have discussed this most carefully in previous numbers of *PROGRESSIVE MEDICINE*.

In a further report Delbet² gives his experiments which seek to prove that some of the weaker antiseptics, such as Dakin's and Labarraque's

¹ Bull. de l'Acad. de Méd., December 21, 1915; review in *Journal of the American Medical Association*, 1916, lxvi, 461.

² *Journal of the American Medical Association*, 1916, lxvi, 522.

solutions, when mixed with the wound secretion, really make a better culture medium. That is, in attempting to kill germs in the wound with hypochlorite, one runs the risk of producing intermediary substances (good culture media) and, in addition, the risk of the suppression of the phagocytosis by the destruction of cells.

Delbet,¹ in a later communication, reports his experiments and clinical experience with the remarkable "cytophylactic" power of a 12.1 to 1000 solution of anhydrous magnesium chloride given intravenously in animals. In man he used it only as a subcutaneous injection and for wound dressings. He is of the opinion that this dressing had such an effect upon the local condition of an infected knee-joint that amputation became unnecessary.

Trémolières and Loew² report their experience with pyoculture in 24 cases. Delbet, in discussing this paper, pointed out that it was not his intention to criticize the opsonic index, but merely to show that it cannot be applied to infected wounds. In addition, pyoculture is simpler, because it is only a question of the presence of bacteria and not of their different kinds. However, Trémolières and Loew make the statement that pyoculture may be positive for some kinds of bacteria and negative for others. This would naturally leave one to infer that a skilled bacteriologist would be helpful in spite of Delbet's statement that with his method of pyoculture such a bacteriologist is not essential.

I know from personal communications that Wright's opsonic index and vaccine therapy was not at all convincing to the majority of surgeons who, in addition to a large experience with infected wounds, understood surgical bacteriology. From what I have read about pyoculture so far, it is not all convincing.

The demand in France for something specific for infected wounds is so great that it is only natural that this something is furnished. Nevertheless, in the endeavor something of real worth may be discovered.

Gas Phlegmons. Fountleroy,³ of the Medical Department of the United States Navy, has made some noteworthy additions to the literature of military surgery. Surgeon Fountleroy had the good fortune to witness and study the medico-military aspects of conditions in and behind the trenches in France. This is reported by the Bureau of Medicine and Surgery of the Navy Department, and published from the Government Printing Office. The book can be obtained by addressing the Surgeon-General of the Navy or a Congressman. In this report, considerable attention is devoted to gas phlegmons.

¹ Bull. de l'Acad. de Méd., September 7, 1915; review in Journal of the American Medical Association, 1915, lcv, 1492.

² Bull. et Mém. de Soc. de Chir., 1915, xli, 1601; review in Surgery, Gynecology and Obstetrics, 1915, xxi, abstr. p. 621.

³ Annals of Surgery, 1916, lxiii, 1; *ibid.*, 1916, lxiv, 136; Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 407.

His second article deals entirely with gas-bacillus infection and was published in January, 1916. The third paper is an address, by invitation, before the American Surgical Association in Washington in May.

The literature on this form of wound infection is tremendous. The observations from the German side are given by Eloesser¹ and Kausch;² from the Russian side, by Shukewich.³

When I compare the experience with gas gangrene in this war with that which I reported seventeen years ago in these volumes, I can find very little, if anything, new in its recognition and treatment.

Many of us always had this infection in mind, and we never neglected to look for emphysema; often the diagnosis was made from the examination of a cover-slip from the wound secretion. We understood the importance of wide-open wound, and at Johns Hopkins Hospital the continuous bath was the usual form of treatment. I get the impression that there were more amputations for compound fractures infected with gas phlegmons in the group then reported than in the present war, but civil surgeons are losing their fear, and are not resorting to immediate amputation, even in compound fracture. Dr. Johnson, of Frederick, Maryland, has just sent me a personal communication of such a case.

By his wide-open wound, he controlled the gas-bacillus infection. Later, he plated the fracture. There was some necrosis of bone, but ultimately a good limb.

In the second place, more cases are reported in which the gas bacillus is obtained from blood cultures. I have been unable to study these cases critically to find out whether many of these patients recovered.

In the third instance, they are finding a number of varieties of gas-producing bacilli, but apparently they all belong to the Welch bacillus group.

QUININE AS A SPECIFIC FOR THE GAS BACILLUS. Kenneth Taylor, working in the Laboratory of the Robert Walton Goelet Research Fund, has done some very important experimental work and has come to the conclusion that quinine hydrochloride may be a specific antiseptic for the gas-bacillus infection of wounds. His first paper appeared September 4, 1915;⁴ the second communication⁵ is dated December 25, 1915. A later paper⁶ was delivered before the Johns Hopkins Medical Society.

Dr. William Welch, in discussing Taylor's paper, seemed to be of the

¹ Journal of the American Medical Association, 1915, lxy, 2001.

² Beitr. z. klin. Chir., 1915, xcvii, 7; review in Surgery, Gynecology and Obstetrics, 1915, xxi, abstr. p. 619.

³ Russk. Vrach, 1915, xiv, No. 45; review in Journal of the American Medical Association, 1916, lxvi, 544.

⁴ Lancet, September 4, 1915.

⁵ British Medical Journal, December 25, 1915; review in Journal of the American Medical Association, 1916, lxvi, 386.

⁶ Johns Hopkins Bulletin, 1916, xxvii, 188.

opinion that it was a real contribution to the therapeutics of this wound infection. Taylor, in his last paper, concludes as follows:

"The gas produced by the bacillus is of little or no importance as a toxic factor.

"The mechanical action of the pressure produced is usually, if not always, the most important part of the infection. To it may be charged the development of highly pathogenic possibilities in a usually rather innocent infection. It brings about (*a*) the death of tissue from the resulting anemia produced by a pressure much higher than that of the circulating blood; (*b*) the actual mechanical fragmentation of the tissue, especially muscle; and (*c*) the mechanical scattering of the infection."

One of the chief problems in the treatment of the infection is that of establishing drainage for the escape of gas before the pressure has resulted in the death of tissue.

Later, I will refer to this paragraph in connection with the treatment of gas phlegmon by the injection of oxygen or hydrogen peroxide.

The solution employed by him is 1 per cent. quinine hydrochloride in cold, boiled water. This solution has been used to wet the dressings, or as a continuous drip; in the latter, it is better to employ a 0.1 per cent. solution to which has been added 0.1 per cent. hydrochloric acid, or 1 per cent. alcohol. In some of the cases, hypodermic injection of the 1 per cent. solution was given into the tissues about the wound.

In his paper published December 25, 1915, he mentions 125 clinical cases and seemed to be impressed with the more favorable course.

In the most recent paper he recommends it as a preventive treatment.

Up to the present time I have not seen Taylor's quinine method mentioned in any contemporary literature. Yet the first publication was in September, 1915, almost one year ago at this writing. It seems to have firmer bacteriological foundation than Dakin's solution, and far more than the use of peroxide.

DANGERS OF OXYGEN INJECTIONS. E. Borchers¹ states that there have been 5 cases of sudden death after the injection of hydrogen dioxide into the tissues in cases of gas phlegmons, and for this reason he advises its discontinuation. He also makes the statement that they are beginning to learn that the prognosis in gas phlegmons is not so grave, and, except in especially severe or very late cases, it is unnecessary to resort to heroic measures.

From the early reports, especially from France, one might have gained the impression that injections of peroxide of hydrogen were specific for the gas bacillus. Now we see that it has its dangers, and then, again, Taylor has pointed out that the chief danger from the gas was due to its pressure. Therefore, such injections would theoretically be harmful.

¹München. med. Wehnschr., 1915, lxii, 1338; reviews in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 268, and Journal of the American Medical Association, 1915, lxxv, 1764.

As far as I can gather, one will have neglected nothing by not employing hydrogen peroxide as a therapeutic agent in any wound infection, and the sooner this is borne in mind the better. Even if it were as economical as sterile water, I am unable to find any evidence to justify its employment. I am inclined to think that it is responsible for some cases of secondary hemorrhage.

INFLAMMABILITY OF THE GAS IN GAS GANGRENE. There is no question that this hydrogen gas in the gangrene burns. I have tested it, and Dr. Dandy, the resident surgeon at Johns Hopkins, also tested it in the most recent case of gas phlegmon. Guéniot¹ recommends this test to differentiate the emphysema of the gas bacillus from that of subcutaneous emphysema. He advises the use of the cautery. In my experience, one can make a little cut under novocaine, and then with the match or cautery ignite the gas. As a matter of fact, the diagnosis in my own cases has always been made from cover-slips, and, as a rule, there is little or no difficulty in differentiating this wound infection from subcutaneous emphysema which is not uncommon after abdominal wounds or wounds of the chest. Many years ago I devoted a great deal of attention to this point, and reported my conclusions in *PROGRESSIVE MEDICINE*.

SERUM THERAPY. M. Weinberg,² of the Pasteur Institute, recognizes two forms of gas gangrene. In the classic type there is marked emphysema, in the toxic form there is extensive edema, often sufficient to mask the gas formation. He is also of the opinion that the gas infection or gangrene is not due to one specific microorganism. The *Bacillus perfringens* (probably identical with the Welch bacillus) is associated with a larger production of gas than the bacillus of malignant edema, and apparently there are other forms of gas bacilli and other varieties of the edematous bacillus. Weinberg also speaks of a new microbe—the *Bacillus fallax*.

Weinberg makes the statement that the results in the treatment of gas gangrene had tremendously improved along with the better development of transportation. Results depend more upon early opening of the wound than upon any other factor. He also reports good results with intravenous salvarsan and superheated air.

In his paper delivered in Glasgow he expresses his conviction that it is necessary to prepare active serum against most of the pathogenic microbes present in wounds, but, unfortunately, the preparation of such sera is not yet completely established. Apparently, it must be a polyvalent serum.

It is interesting to note here that in the English army they are employ-

¹ Bull. de l'Acad. de Méd., September 7, 1915; review in Journal of the American Medical Association, 1915, lxxv, 1492.

² Lancet, 1916, cxc, 622; review in Surgery, Gynecology and Obstetrics, 1916, xxiii, 64; and Glasgow Medical Journal, April, 1916.

ing a polyvalent serum of typhoid and of a number of strains of paratyphoid. As yet a protective serum for the different forms of dysentery is not completely worked out. Adami writes me that at the present time the injection of the protective serum against dysentery is so painful that it is employed only in selected cases.

GAS BACILLUS IN AMPUTATED STUMP. Piper¹ records this interesting case. The left leg had been amputated without flaps and the wound was not closed, but the right leg had been amputated, the wound packed with gauze, and the flaps sutured over the packing, apparently for hemorrhage. When this patient was admitted to the ward of the American Ambulance a few days after the amputation, there was gas infection in the stump packed and partially sutured. Instead of reamputating at once, Dr. Hutchinson decided to try irrigation first; stitches and packing were removed. The patient recovered, and the stump healed by granulation about the protruding bone.

This case demonstrates that gas infection will rarely attack the stump of an amputation through healthy tissue, unless there is a foreign body (gauze) or a closed wound.

In 1899 I² reported a somewhat similar case. The patient's left leg had been amputated below the knee for a compound fracture, crushing the leg above the ankle. The amputation had been performed immediately after the injury, at the side of the railroad track, with little or no surgical precautions.

Upon admission to Johns Hopkins Hospital, six hours later, the closed stump was distended with blood. I anesthetized the patient, put on an Esmarch, opened the wound, turned out the blood-clot, ligated the two main vessels. There was absolutely no evidence of gas or infection. The wound was irrigated with 1 to 1000 bichloride, and closed.

Five hours later the patient complained of chill and intense pain and heat in the stump. The temperature rose to 104°, the pulse to 150. The stump was so painful that he was given a little ether for the dressing. Upon examining it, emphysema was present to 1 cm. above the patella; red, irregular lines of lymphangitis extended up the thigh. Upon opening the wound, there was a little blood-stained serum, but no gas bubbles. But cover-slips from this material demonstrated a large bacillus which later cultivation proved to be the gas bacillus. On making a longitudinal exploratory incision we found all the tissue between skin and bone below the knee separated by an emphysematous exudate. For this reason the leg was amputated above the knee, slightly beyond the zone of emphysema. The patient with the open stump was placed in a continuous bath. He recovered without further signs of infection.

This demonstrates that a thorough disinfection of the wound is of little value if the wound is closed. If the surgeon who first amputated

¹ Loc. cit.

² PROGRESSIVE MEDICINE, December, 1899, p. 164.

the leg had left the wound open, or if I had left the wound open when I removed the blood-clot, the probabilities are there would have been no indication for a secondary amputation.

It is quite possible that my secondary amputation was unnecessary. Perhaps I should have tried free incisions, open wound, and continuous bath or irrigations first. But the local signs of emphysematous cellulitis were so diffused in this stump, and the patient's general condition looked so septic, that I feared to delay or compromise.

X-RAY DIAGNOSIS IN GAS PHLEGMON. In 1915 Payr¹ demonstrated that with the x -rays one might be able to distinguish, from the position of the gas bubble, whether the gas phlegmon was deep or superficial. He discussed a number of such cases.

Davis,² of Chicago, writes of his experience in a base hospital with the British army in France. Routine x -ray pictures are taken from two directions. From these one can note the presence or absence of a foreign body, its location, and, as a rule, can make out the condition of the tissue about the foreign body. Pus and gas also produce their shadows. From these pictures, Davis believes the surgeon has information which is of great help to him in the operative treatment.

Tetanus. There is uniformity of appreciation of the protective value of the antitoxin for tetanus. I cannot find a dissenting opinion. The reverse is true when we read the literature on the treatment of tetanus after the clinical symptoms have manifested themselves. Beginning in 1900, I³ presented the literature on this subject, and have continued it at intervals ever since.

Therefore there has been no change, but this war has given surgeons a larger experience in the actual treatment. Apparently, the majority agree on the importance of repeated large doses of the antitoxin subcutaneously. There is not such uniformity of opinion in regard to the intraspinal administration, nor about the injections of magnesium sulphate into the spinal canal.

All agree, however, that in the treatment of tetanus more than one drug should be employed. There is, first, the specific treatment with the antitoxin. All other drugs may be classed as agencies for symptomatic treatment—magnesium sulphate, chloral, morphine, bromides; absolute rest and quiet. There is still a number of authorities who believe in using carbolic acid locally in the wound; others advise chlorinated lime; still others ultraviolet rays. An excellent summary will be found in the *Journal of the American Medical Association* (Therapeutics, 1915, lxx, 2086).

Auregan⁴ gives his experience with colloidal iodine and serum. Her-

¹ Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 81. ² Ibid., p. 635.

³ PROGRESSIVE MEDICINE, December, 1900, p. 126.

⁴ Lancet, February 27, 1915; review in Journal of the American Medical Association, 1915, lxiv, 1196.

cher¹ employs intravenously a solution of ether salt; Lumière,² sodium persulphate.

I would advise the reading of the most recent contribution of Meltzer³ for the details of the employment of magnesium sulphate. His summary is as follows: In every case of tetanus give 1.2 c.c. of a 25 per cent. solution of magnesium sulphate subcutaneously three or four times a day until all symptoms have disappeared.

When there are severe tetanic attacks give 1 c.c. of the same 25 per cent. solution for every twenty pounds of body weight (in adults) by the intraspinal method. When the tetanic complications threaten life, give intravenously 2 or 3 c.c. of a 6 per cent. solution per minute until the tetanic convulsions subside and respirations become shallow and slow.

When the respirations are too slow and seem impaired, give calcium chloride, using the same intravenous cannula through which the solution of magnesium sulphate has been running. Give a small amount of a 2.5 per cent. solution. In using the calcium chloride be very careful not to give too much, or to counteract the good effect of the magnesium sulphate.

This report of Meltzer demonstrates that the magnesium sulphate method is a delicate procedure and not devoid of danger. But we must realize that the danger of the tetanus convulsions untreated is greater than that of magnesium sulphate.

Meltzer also advises to have on hand, ready for use, an intrapharyngeal insufflation apparatus.

Kocher⁴ uses a 15 per cent. solution intraspinally; otherwise his directions seem identical with those of Meltzer. He reports good results in adults and poor ones in children. The effect of an intraspinal injection lasts from eight to twenty-four hours; it should not be repeated more than twice in twenty-four hours.

LATE TETANUS. The more recent literature on this rather unusual manifestation is recorded by Bérard,⁵ Bérard and Lumière,⁶ Teutschländer⁷ and Barling.⁸

¹ München. med. Wehnschr., 1915, lxii, 1126; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 277.

² Lyon Chir., October, 1915; review in Journal of the American Medical Association, 1916, lxvi, p. 152.

³ Journal of the American Medical Association, 1916, lxvi, 931.

⁴ Bürgi, Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 74.

⁵ Bull. de l'Acad. de Méd., 1915, lxxiv, 234; review in Surgery, Gynecology and Obstetrics, 1915, xxi, abstr. p. 629.

⁶ Lyon Chir., 1915, xii, 404; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 276.

⁷ Deutsche med. Wehnschr., 1915, xli, 1453; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 402.

⁸ British Medical Journal, 1916, i, 337; review in Surgery, Gynecology and Obstetrics, 1916, xxiii, abstr. p. 58.

Speed¹ reports on postoperative tetanus and Mouchet² on chronic recurrent tetanus. Then there is an interesting article by Phocas³ on the flaring up of the latent infection in wounds of war disturbed by surgery.

These conditions must not be forgotten. The evidence shows that in the majority of gunshot wounds the bacillus of tetanus, that of Welch, other bacilli, and the streptococcus are always introduced at the time of the injury. The only protective serum so far is that for tetanus. The wound may heal, but if, during the healing process, there is any sudden rise of temperature, immediately give the patient another protective dose of the antitoxin. If operations are indicated after the apparent healing of the wound, with and without residual sinuses, it would probably be safer to give the patient a protective dose of the antitoxin, and in operations use antiseptics and provide for temporary drainage. The number of such cases is comparatively small, but a little forethought will protect them.

Erysipelas. While references to tetanus and gas gangrene are numerous, I find only one to erysipelas as a complication of gunshot wounds, by Jochmann.⁴ The author has found that this complication is very rare, but the mortality is higher than from erysipelas in civil life. In treatment, the simplest measures seem most effectual. The disease runs its course, there seems to be no specific remedy for it, and it is simply a question of making the patient comfortable and supporting his general condition. Jochmann is of the opinion that the antistreptococcus serum has no special influence on the local process, but apparently improved the pulse and the mental condition of the patient.

I have read recently a long report summarizing the cases of erysipelas in Bellevue Hospital in New York, but the reference has been lost. The conclusions were identical with those of Jochmann. No treatment was found to have influence on the local course of the disease. The different localizations and types of erysipelas had different periods of duration.

In view of the fact that the majority of gunshot wounds are infected with streptococci, it seems strange that erysipelas should be so infrequent. One naturally asks, is erysipelas due to a special kind of streptococcus?

In glancing over my index to the literature on erysipelas since 1906, I find rather few references. Most of them have to do with some specific treatment. For example, in 1906 Noguera⁵ claimed that rose-water,

¹ Surgery, Gynecology and Obstetrics, 1916, xxii, 443, 496.

² Medical Press and Circular, 1916, ci, 28; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 521.

³ Journal of the American Medical Association, 1915, lxx, 2021.

⁴ Deutsche med. Wchnschr., November 17, 1914; review in Journal of the American Medical Association, 1915, lxiv, 184.

⁵ Zentralbl. f. Chir., 1906, xxiii, 372.

glycerin and salicylic acid accomplished a cure in some 82 cases of erysipelas in from three to six days. The report from Bellevue Hospital shows that the average duration of erysipelas of the face when left alone, is from three to six days.

Then, the most recent contribution by Magi¹ claims brilliant effects from iodine.

When I was resident at Johns Hopkins Hospital I went over the histories of all the cases of erysipelas and streptococcus infection on record in the surgical clinic from 1889 to about 1898. I was struck, first, by the low mortality; second, in going over the autopsies of the cases who succumbed to the infection, I found that without an exception the individuals were handicapped by some chronic condition of the heart, lungs, kidneys or arteries which interfered with elimination, and quite a few were diabetics and chronic alcoholics. In healthy individuals, therefore, an attack of erysipelas is not a serious affair. From this experience, I was impressed that wet applications, usually hot, were most comfortable of all. We found that if we painted the skin with collodion we got the best results from the hot applications—really a method of applying dry heat, which is nothing new.

I also demonstrated in this investigation that when a case of erysipelas, or severe streptococcus infection, was admitted to one ward, other cases developed in open granulating wounds, and there were a few operating-room infections. After as careful an investigation as was possible to make, there seemed to be but one avenue for spreading the infection, and that was the hand of the individual carrying the dressing case. Since the introduction of gloves and the dressing of the wound with the gloved hand or with instruments only, while cases of erysipelas and streptococcus infection are still being admitted to the ward, other cases are infected only with the rarest exceptions.

The last case of erysipelas observed in the wards of St. Agnes' Hospital well illustrates the attitude of a recently trained surgeon to a rare wound infection. When I first saw the patient he had been painted with iodine almost from head to foot, and about every three to five days at the height of the fever of a recurrent attack of the creeping erysipelas, I was hurriedly called with the information that the patient was dying. The individual had apparently no chronic diseases; the erysipelas had started in a large open wound on the face; he recovered from both, the erysipelas and the applications of iodine. I am quite certain that in this case the iodine showed no evidence of being specific. It apparently did not add to the discomfort. This patient was in a small room with two beds adjoining the main surgical ward. He was taken care of by individuals who always wore gown and gloves. No other cases developed in the hospital.

¹ Policlinico, April 18, 1915; review in *Journal of the American Medical Association*, 1915, lxiv, 1951.

NERVES.

Injuries of Nerves. The function of a nerve may be temporarily interrupted without any tearing of the nerve trunk proper. The loss of function is usually partial and is restored within three weeks.¹

When the nerve is partially or wholly divided, the sooner an operation is performed, the better. Operation, when the wound is septic, is contra-indicated.

Operations, even after months of delay, may be successful.

This expresses the entire problem as far as indications for operation are concerned.

First, we wish to recognize those cases in which, although function is absent, yet there is no absolute injury to the nerve trunk. Then, again, how long shall we wait with operation when the wound is still granulating? When is an open wound not septic?

Marburg and Ranzi² express the opinion that in suppurating wounds there should be several weeks' delay, but they do not advise waiting until the wound is entirely healed.

Operation is indicated when there is loss of motion and sensation, and complete lack of electric reaction, or the electric reaction is growing worse, or the reaction of degeneration remains stationary.

NERVE CONCUSSION. There is a number of reports of cases with all the signs of a nerve injury, yet, the exploratory operation has been unable to demonstrate any rupture.

Tubby³ dwells especially on this rather vague group. The loss of function might be explained by hemorrhage, or temporary anemia, or hyperemia.

Perthes⁴ reports a case of paralysis of the brachial plexus in which the bullet wound was in the shoulder without any demonstrable injury of the nerve trunk. He speaks of it as indirect effects of gunshot wounds on nerve tissue.

FIXATION. Lyle,⁵ of New York, from his experience in the American Ambulance Hospital, lays especial emphasis upon the fixation of the limb from the moment of the injury, and calls attention to the fact that many cases of apparent nerve injury may recover without exposure of the nerve.

In all bullet wounds, after attending to the wound itself, never neglect to search for signs of nerve injury; never neglect, if possible, an x-ray;

¹ Stoney, *British Medical Journal*, 1915, ii, 10.

² *Wiener klin. Wehnschr.*, 1915, xxviii, 611; review in *Surgery, Gynecology and Obstetrics*, 1915, xxi, abstr. p. 529.

³ *British Medical Journal*, 1915, i, 57; review in *Surgery, Gynecology and Obstetrics*, 1915, xx, abstr. p. 520.

⁴ *Deutsche Ztschr. f. Chir.*, 1915, cxxxii, 191; review in *Surgery, Gynecology and Obstetrics*, 1915, xx, abstr. p. 173.

⁵ *Surgery, Gynecology and Obstetrics*, 1916, xxii, 127.

always bear in mind that upon the injured nerve there may be a loose bone body. The proper immobilization and treatment of a fracture may prevent the nerve from being caught in callus and scar tissue.

Lyle also goes into the detail not only of the necessity of the proper position of the extremity, but of the care of the paralyzed muscles until nerve function is restored.

One gets the impression that wounds of this kind demand unusual attention, and a larger staff of helpers. Generally, there is a wound requiring daily, or more frequent, dressing; an extremity demanding an

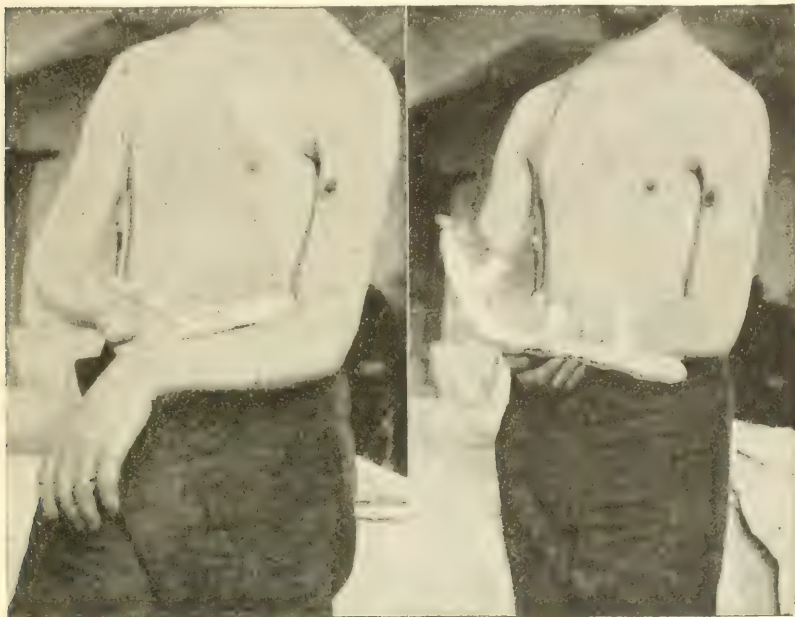


FIG. 46 (at left).—Perforating bullet wound of the soft parts at the level of the deltoid. Note drop-wrists. (Lyle.)

FIG. 47.—Same case as Fig. 46, treated by the hyperextension method. Shows a temporary splint used while the Tuffier splint is being made. There is an error in this picture, as the splint is too long and there should be only one strap, that at the wrist. (Lyle.)

adjustable fixation splint, meeting the indications of the fracture and the nerve injury; then, very shortly, there must begin daily massage, the warm baths and electric treatment. Lyle emphasizes that it is important not to depend upon electric stimulation only.

Then, in addition, there is demanded frequent electric examination to ascertain the exact character of the nerve injury and its extent.

In civil practice we get very little experience with nerve injuries. As a rule the wound is clean-cut, and the operation can be performed at once. Lyle, more than any other reporter, pictures the difficulties in

the treatment of wounds of this character and of the importance of not neglecting any of the different procedures. It is not operation alone that shortens the disability and promises the greatest restoration to full function, but a very complicated system of treatment requiring patience, industry, and special training. How few of our hospitals in time of peace are prepared for such cases:

According to Lyle, the principle of fixation is, that the paralyzed muscles must be held in a position of relaxation and protected from strain, and this postural prophylaxis should begin at once and continue to the end. Figs. 46 and 47 picture the principles of this fixation.

From my observations in civil hospitals, I agree with Lyle that this essential principle, which is common in all wounds, does not receive the proper attention. We might say that, in the great majority of hospitals today, wounds are dressed and fractures are fixed, but little or no attention is paid to the maintenance of joint function, muscle tone, and the general condition of the patient, until after three or more weeks the local and general condition has reached such a stage that the physician or surgeon is practically forced to give it thought and adopt some form of treatment.

INDICATIONS FOR OPERATION. Bruns¹ writes, from his experience with 376 nerve injuries, and classifies them into three groups: In the first group there is complete paralysis, sensory and motor, and reaction of degeneration. Yet he is of the opinion that it is impossible to tell whether this is due to complete rupture, or scar-tissue pressure. If, during the period of waiting, there is marked improvement, delay operation; if not, explore the nerve as soon as the wound is healed and the fracture united.

This remark of Bruns indicates how difficult it is to ascertain, from the clinical history and examination, the exact nature of the nerve injury.

In his second group some muscles are not paralyzed; only the paralyzed muscles show reaction of degeneration. Delay operation longer in this group, as many cases spontaneously recover.

In the third group the reaction of degeneration is partial. Here first try electricity and massage: if there is much pain, explore the nerve and isolate it from scar tissue. He has observed 33 cases recovering without operation and great improvement after neurolysis in 13 cases.

TIME TO OPERATE. There is uniform agreement that, in the usual bullet or gunshot wound, immediate operation is out of the question on account of the character of the wound, but beyond this there seems to be the greatest difference of opinion as to how long to wait. Schiffbauer² quotes Oppenheim as advising three months' delay, Rothman eight months. Schiffbauer is of the opinion that in a simple bullet wound the

¹ Review in *Surgery, Gynecology and Obstetrics*, 1916, xxii, abstr. p. 290.

² *Surgery, Gynecology and Obstetrics*, 1916, xxii, 133.

nerve may be explored in from three to six weeks, while in infected wounds one must wait until there is complete healing which usually requires six to eight weeks. In 1914 I¹ reviewed a number of articles on nerve injuries in civil life with regard to this point of time. Lexer believed that in a nerve injury associated with fracture, the results of suture are not impaired by a delay of from four to six weeks. However, the larger number of authorities were of the opinion that the sooner the nerve is exposed the better.

I have had no experience to mention with nerve injuries, but I gather from this tremendous new material that the results, on the whole, are pretty bad. Now, if there were any method of treatment which would yield 100 per cent. of recoveries there would be no difficulty, but it seems impossible to ascertain the factor or factors which explain the failure to restore function in a nerve after the operation of suture. I get the impression that the longer the delay, the greater the difficulties, and, naturally, the poorer the results.

Ferrand² states that the operation should never be done until after two months or longer.

Sicard³ waits three months.

INTRANEURAL INJECTIONS FOR DIAGNOSIS AND TREATMENT. Hofmeister,⁴ in his elaborate article, recommends the intraneural infiltration of the nerve with weak solution of novocaine and adrenalin. In the first place, the rapidity with which the nerve becomes infiltrated gives a pretty good idea of its condition. The atrophic peripheral portion infiltrates easily; dense scar tissue with the greatest difficulty. After a time one becomes quite expert with this test. Then the infiltration enlarges the size of the nerve—temporarily, it is true, but this may have a good effect on the endoneural scar tissue, tearing it and freeing the nerve fibrils. The larger nerve may protect itself from future contraction of the surrounding tissue. Then, the adrenalin protects the nerve from hemorrhage in the surrounding parts. Hofmeister was led to try this in war surgery from a few past experiences in times of peace. He states that he has never seen any harm even after injecting a normal motor nerve.

I know that I paralyzed a motor bundle in the brachial plexus by the injection of 1 to 400 novocaine. It was during an operation for extensive cancer; the muscles were immediately paralyzed and there was little or no regain in power during the four months the patient lived after operation. I was operating under local anesthesia, and made the injection for the relief of pain.

¹ PROGRESSIVE MEDICINE, December, 1914, p. 273.

² Journal de Rad., 1915, i, 629; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 274.

³ Surgery, Gynecology and Obstetrics, *ibid.*, abstr. p. 275.

⁴ Beitr. z. klin. Chir., 1915, xevi, 329.

It is quite possible that I used too much force in the infiltration. It seems to me that Hofmeister expects too much from his intraneural infiltration.

EXPLORATORY OPERATION. A large number of surgeons, especially as their experience is increasing, are advising the exploration of the apparently injured nerve under local anesthesia in order to ascertain the exact local condition.

Delorme¹ advises this exploratory incision within two or three weeks after the injury. Legueu agrees with him.

Wilms² is of the opinion that when the condition of the wound does not contra-indicate an early operation upon the nerve, but when it is difficult to tell whether an operation is indicated or not, the nerve should be explored under local anesthesia.

OPERATIVE METHODS. The bridging of the gap will be discussed in the next paragraph. Schiffbauer³ states that, in general, there should be accurate coaptation of the severed nerve ends, aseptic healing and no hematoma. It seems to me that this is possible only when the nerve can be explored at once after the injury, and when there is no infected wound. In these gunshot wounds of nerves, the chief difficulty is scar tissue. Schiffbauer, and the majority of surgeons, do not use the Esmarch. Bleeding points should be tied, but when there is bleeding from the cut nerve, try pressure first, before ligature.

In making the incision, place it so the central portion of the trunk of the nerve is exposed first, then proceed to the scar tissue; remove the scar tissue, except that which might be the nerve trunk, or the scar tissue between the nerve ends. The injection of a weak solution of novocaine brings out the gross appearance of the nerve trunk and shows how much it is involved in scar tissue. One can also, with the knife, divide the perineurium. In cases of this kind there is an apparent intact nerve trunk imbedded in scar tissue, but we must always bear in mind the possibility that, in addition to pressure from scar tissue without, there may be scar tissue within the nerve trunk.

If one can demonstrate that the nerve ends are separated and there is a bridge of scar tissue, the most important point is to isolate the normal trunk on each side of the scar defect. Then one should make an electric examination, because there may still be intact fibrils in this scar tissue. Then, again, one must be most particular in isolating the trunk above and below, in order not to injure any branches. From this point, Schiffbauer is somewhat indefinite as to the dissection of the scar tissue. Of course, if one can resect and bring the ends together, this should be

¹ *Rev. de Chir.*, 1915, xxxiv, 402; review in *Surgery, Gynecology and Obstetrics*, 1916, xxii, abstr. p. 399.

² *Deutsche med. Wchnschr.*, 1915, xli, 1417; review in *Surgery, Gynecology and Obstetrics*, 1916, xxii, abstr. p. 400.

³ *Loc. cit.*

done, provided it can be demonstrated that the nerve has been ruptured and its ends are separated, and if we can suture the two ends together. We then have a simple case. But when there is a defect, how shall it be bridged?

Tuffier¹ reports his experience with Dumas in 280 cases. As in their opinion resection and nerve suture offered less possibility of a cure than any other method, they performed it in 19 cases only, with not a single result.

Their scheme seems to be to liberate the intact nerve from the scar tissue; to handle the nerve as gently as possible; never to make exploratory incisions into the nerve, even if there is evidence of scar tissue; and to leave a bridge of scar tissue about the size and shape of the nerve trunk between the severed ends; then surround the isolated nerve trunk with transplanted fat. In 173 cases this method was employed apparently with a large number of good results.

BRIDGE FOR THE GAP IN NERVE SUTURE. L. Edinger² employs for this purpose an artery filled with agar jelly. One hundred of these tubes have already been distributed to the operating neurologists among the German surgeons. Ludlow has employed the jelly tube in fourteen cases. The gaps measured from 5 to 15 cm., and in every case there is now evidence of nerve regeneration. Edinger is of the opinion that the regenerating nerve fiber at first is like a jet of thick fluid. Therefore it is turned aside by the smallest obstacle. A tube of this kind, theoretically, should be ideal.

When one is able to suture a nerve immediately after the injury, when there has been as yet no contraction and no scar tissue, direct nerve suture is a fairly simple operative procedure. But after large accidental wounds and especially in wounds in war, the nature of the wound prohibits immediate operation in the first instance, and the infection of the wound delays it in the second instance. Then when we operate and finally have isolated the nerve there is usually a gap; if not, the condition of the nerve at the point of injury is so distorted by scar tissue that resection offers greater hope of a result than simple separation. Therefore in military surgery we may be confronted with many cases of nerve suture in which there is a gap. Other observers, who have used fascia and fat, apparently have not had as good results as those just reported with the jelly tube. Apparently, tubes of this kind should not be difficult to make, in fact, one could obtain them from a cat the morning of the operation. In an emergency, one could take the saphenous vein from the patient and get the agar jelly from the bacteriological department.

¹ Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 67.

² Münch. med. Wchnschr., February 15, 1916; review in Journal of the American Medical Association, 1916, lxvi, 968, 1064.

In a previous paper, Edinger¹ filled the artery with embryonic nerve tissue. The review states that a material similar to this has been constructed by him from silicic acid. He seems to be of the opinion that the axis-cylinder will grow through material of this kind better than through anything else. Later, apparently, he substituted the agar-agar.

Steinthal,² in going over the literature relating to some tubular foreign substance in bridging nerve defects, concludes that there is little evidence in its favor. He does not consider the experience of the present war.

Hofmeister³ reports a case in which he covered the ends of the divided and sutured nerve with a transplanted vein. Five months later the wound was re-explored, because there was no return of function. The nerve within the vein was entirely converted into scar tissue, no axis-cylinders remained.

Steinthal agrees with Braun that the method of employing any foreign tissue or body as an aid to nerve regeneration is entirely in its experimental stage, and even if some cases are successful in animals, that is no reason why they would promise any success in the connective-tissue wound which complicates the nerve injury in military surgery.

NERVE-GRAFTING AND IMPLANTATION. Schiffbauer⁴ refers to the work of Borchard and Hofmeister. The former, after resecting 10 cm. of the musculospiral nerve, implanted the central and peripheral ends into the maculocutaneous nerve. In this case in nine months the triceps and supinator regained function, the abductor pollicis slight function, the extensors no function. Hofmeister reports a number of nerve implantations, double and triple. Schiffbauer must have had pretty simple cases, because he had to graft but once. In this case the central end of the ulnar was grafted into the median nerve and the peripheral nerve into the same nerve below. There was no injury to the function of the median nerve. The result is not noted.

Weible⁵ reports a case in which there was a defect of about 13 cm. in the median and ulnar nerves. The injury had been a huge lacerated wound from the moving knives of a moving machine. He split both the proximal and the distal portions of each nerve down to the torn ends which were occupied by neuroma. He did not remove the neuroma. Function was gradually restored, of the ulnar nerve apparently completely, of the median partially.

This is the only case which I can find in which the neuroma was not removed. The defect was bridged by nerve tissue; there was a clean wound. A case of this kind speaks well for this method of bringing the

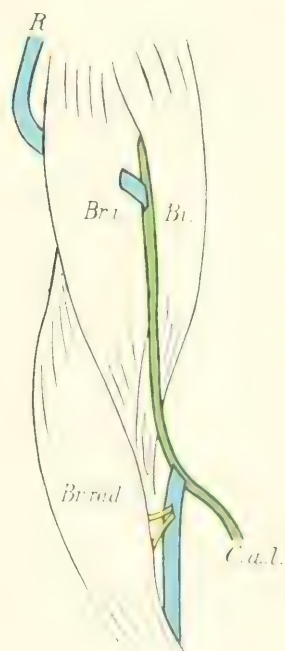
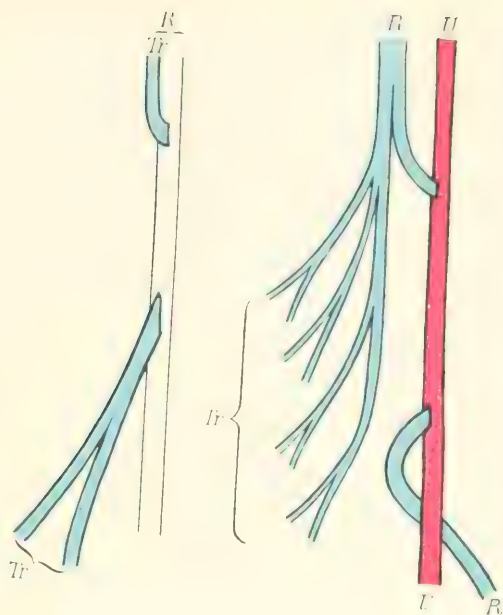
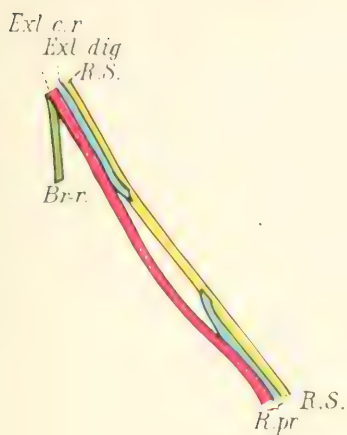
¹ Münch. med. Wchnschr., February 15, 1916; review in Journal of the American Medical Association, 1916, lxvi, 968.

² Beitr. z. klin. Chir., 1915, xevi, 295.

³ Loc. cit.

⁴ Loc. cit.

⁵ Review in Journal of the American Medical Association, 1915, lxiv, 776.





defect. There is no note that he used any transplanted tissue to prevent adhesions forming about the nerve.

A somewhat similar plastic operation I¹ reported in 1909 (Fig. 48). This case, operated on by Mackenzie, of Portland, Oregon, has almost complete restoration of function.

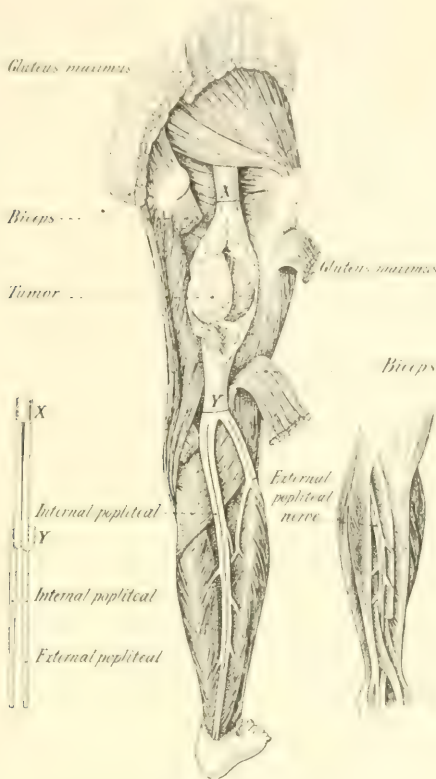


FIG. 48.—Diagram to show the position of the tumor, the part resected, and the method of division of the internal and external popliteal nerve; also the scheme of suture. (Sketch by Miss S. Hayes.)

Delorme² also recommends this plastic operation to bridge large defects.

For the fully developed method of grafting the proximal and distal end on an uninjured nerve in the neighborhood, one should turn to the splendid work of Hofmeister,³ from which I reproduce one characteristic illustration (see colored Plate).

This method has the great advantage of practically side-tracking or

¹ PROGRESSIVE MEDICINE, December, 1909, p. 208, Fig. 31.

² Review in Journal of the American Medical Association, 1915, lxiv, 861.

³ Beitr. z. klin. Chir., 1915, xevi, 329.

isolating the old wound in which the injured nerve rested. Apparently, the greatest obstacle to the restoration of nerve function in gunshot wounds is scar tissue. It seems almost impossible to prevent its reformation before the axis-cylinders have a chance to reform, and even if they succeed they are later blocked again by scar contraction. Of all the methods, this one impresses me as the best. We know that it does not harm the uninjured nerve. If it should fail, we would have little difficulty in finding the ends again for the trial of another method.

OPERATION ELECTRODE. Marie¹ has devised an electrode which can be sterilized and employed during operation after the nerve is exposed, to test its function and help in deciding what operation is indicated.

GROSS PATHOLOGY. Schiffbauer² states that in the majority of cases neuromata are found. The amount of scar tissue varies tremendously. It is very difficult to tell, when the nerve is imbedded in scar tissue, whether the trunk is partially or completely severed, or whether it is simply caught in scar tissue. As a rule a careful investigation of the history before operation will allow one to distinguish between complete rupture of a nerve and secondary pressure from scar tissue. Yet, we must recollect that the paralysis of the primary confusion may not recover before the nerve is compressed by the contracting granulation tissue.

Quénu, a French surgeon, is of the opinion that it is impossible to recognize with the naked eye whether the nerve is intact or not.

The best contribution to the actual findings in and about the injured nerve in gunshot wounds of the present war is that by Heile and Hezel.³ There are sixteen plates with the article. The authors are anxious to record each one of their cases in the greatest detail, and later, when sufficient time has elapsed, to make a similar detailed study of their results.

In the large majority of cases of bullet and gunshot wounds there is only a partial separation of continuity of the fibrils in the nerve trunk. The rest of the harm is due to peri- and endoneural connective-tissue reaction. But the recognition of that portion of the trunk in which the nerve fibrils are actually lacerated is very difficult.

Völcker⁴ gives a very good description of the operative findings in about 16 cases, with 21 diagrammatic illustrations.

MICROSCOPIC PATHOLOGY. Borchardt⁵ reproduces histological pictures of cross-sections of nerves which in the gross appeared normal, but in the section showed evidence of scar tissue in place, with complete

¹ Review in Journal of the American Medical Association, 1915, lxiv, 1112.

² Loc. cit.

³ Beitr. z. klin. Chir., 1915, xcvi, 299.

⁴ Deutsche Ztschr. f. Chir., 1915, cxxxiii, 65.

⁵ Beitr. z. klin. Chir., 1916, xcvi, 233; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 233.

destruction of the axis-cylinder. Nevertheless, Borchardt agrees with Cassirer that there is no indication to resect such nerves. He sees no objection to resection, providing the ends can be brought together, but if such resection leaves a defect, it is wiser to bring together a nerve trunk of this kind than to trust to any method of bridging the defect. Borchardt is an advocate of early operation.

OPERATIONS FOR PAINFUL NERVE INJURIES. Walther,¹ in cases of nerve injury with intense pain, recommends an earlier operation than in cases of paralysis without pain. He does not even wait for the healing of the wound, but explores and isolates the nerve. During his operation he keeps his wound constantly wet with salt solution.

The case reported by Thieman² is rather remarkable. There was paralysis of the foot, with intense and continuous pain associated with a gunshot wound near the knee; 3 cm. of the nerve involved in scar tissue was resected, with suture of the stump. Pain was relieved at once, and motion was beginning to return at the end of the third week.

NEUROLYSIS. Stoffel³ is an advocate of perfect approximation when there is resection and suture, and a much more painstaking technic when the nerve is free. He is of the opinion that many of the failures are due to the presence of endoneural scar tissue and few surgeons pay any attention to it. He dissects first the perineural scar; then he palpates the nerve trunk; if he feels any areas that are hard, he separates these bundles. He says the technic requires considerable skill, but he attempts to remove or separate all the endoneural scar tissue. Then he envelops the nerve in calves' arteries hardened in formalin, and, more recently, in the peritoneum from calves hardened in the same way. The isolated nerve should, if possible, be relaxed. In some cases he resects and sutures part of the trunk, and performs neurolysis on the remainder.

One gets the impression that there is a good deal of fancy about this technic and the removal of endoneural scar, and I note that a number of German surgeons question the necessity for Stoffel's technic, as well as his statement as to the importance of accurate apposition after resection.

ULTIMATE RESULTS. In the reading of reviews and original articles on the more recent war surgery, one gets the impression that successful cases have been observed after almost all possible types of injury, and after all methods of operation. Function has returned after isolating the nerve, after resection and direct suture, after filling the defect in various ways, after grafting and implantation. The return of function varies as to time and completeness. In one of Müller's⁴ cases it was

¹ Jour. Amer. Med. Assn., 1915, lxiv, 68.

² Review in Jour. Amer. Med. Assn., 1915, lxiv, 2027.

³ Review in Surg., Gynec. and Obst., 1916, xxii, abstr. p. 68.

⁴ Beitr. z. klin. Chir., 1915, xcvi, 263; review in Surg., Gynec. and Obst., 1916, xxii, abstr. p. 400.

eleven months before there were any signs of returning function, and then return was rapid.

Sicard has never observed restoration of function in cases of suture after complete destruction of the nerve trunk, in which clinically there had been total motor paralysis and total reaction of degeneration. This statement is made after an observation of more than one year in some cases. One naturally asks, is this due to the delay of three months or to technic?

Another French surgeon, Ferran,¹ expresses the opinion that when there are signs of complete motor paralysis and anesthesia, and complete reaction of degeneration as well as signs of trophic disturbances, it is a question whether operation offers much hope. Ferrand has rarely seen results after resection and suture. For this reason, if he does operate, he is rather inclined to leave the scar bridge alone.

Bruns² states that he has had 10 successful cases after resection and suture.

Borchardt,³ from his experience up to 1915, was not particularly pleased with his operative results in 70 cases. He mentions, however, three excellent results after nerve suture with complete restoration of function. Apparently, Borchardt also believes in retaining scar tissue rather than leaving a defect that must be bridged. He sees no objection to resecting the scar tissue, providing direct end-to-end suture can be done.

Grosse⁴ found that his good results were in nerves of the upper extremity, and that function was restored in from three weeks to seven months. In the first 20 cases there were 6 failures, about one-third. In the remaining 17 cases, the time is not sufficient, but, so far, there are 12 failures.

Thöle⁵ goes very carefully into the results after 46 operations. In 11 cases of complete severing of the nerve, the ends were freshened and sutured; in only 4 of these 11 cases was there any improvement at all, and in these none with complete restoration of function.

It is very important to note that in 10 cases in which there was not complete severing of the nerve trunk, but only a spindle-shaped thickening, this area was resected; so far, there is improvement in but two of these cases.

I get the impression that nerve trunks of this kind should not be resected.

¹ Loc. cit.

² Berl. klin. Wchnschr., 1915, lii, 989; review in Surg., Gynec. and Obst., 1916, xxii, abstr. p. 290.

³ Review in Surg., Gynec. and Obst., 1916, xxii, abstr. p. 66.

⁴ Ibid., xxii, abstr. p. 67.

⁵ Beitr. z. klin. Chir., 1915, xcviii, 131; review in Surg., Gynec. and Obst., 1916, xxii, abstr. p. 513.

There is one slight improvement among 5 cases in which the gap has been bridged by flaps from the peripheral end of the wounded nerve.

CONCLUSIONS. I have made an exhaustive, although perhaps rapid, summary of a large number of contributions to the surgery of gunshot injuries of nerves. I have given the impression of surgeons in every army. The majority of the contributors are well known and were familiar with the meager experience of nerve surgery in time of peace. All express the opinion that the excess of scar tissue is the chief obstacle to restoration of function. All agree on the difficulty of the neurological interpretation, and the difficulty, even after the nerve is exposed, to tell the exact extent of the injury. When it comes to operative interference, there is great difference of opinion, but the time is too short since the beginning of the war to really know what the ultimate results will be.

The number of this type of injury seems relatively large. In addition to this, it is a very important group from an economic standpoint. Motor paralysis incapacitates. Then, there is a large number of patients who suffer pain which, if not relieved, will interfere with their ability to work. It is still too early to feel convinced that the favorable results so far recorded in the painful cases will remain so after further observation. I am chiefly impressed with the importance of a thorough exploration of the nerve. Every method of examination should be employed before resection. One must be quite sure that there is total destruction before resection is resorted to. When there is no resection, or only a partial one, the most important part of the treatment is the prevention of secondary compression from the scar in the healed wound. If one cannot transplant the nerve into healthy muscle, it would seem best to transplant fat about the nerve. When the nerve must be resected, I am most impressed with Hofmeister's results in nerve implantation.

Apparently, there has been great disappointment in the application of knowledge obtained by experimental work on animals to the actual surgery of injured nerves in gunshot wounds. All methods which are helpful in obtaining complete nerve regeneration in animals rarely succeed in the different character of the wound, in the soldier's injured tissues.

We may end by saying that nerve surgery is in its experimental stage in spite of the huge experience of the recent war.

Alcohol Injections in Painful Neuritis. We know, from Mitchell's experience in the Civil War, the terrific pain which may occur after certain kinds of gunshot wounds. Sicard¹ has had an experience with 21 cases of what he calls painful neuritis. All ordinary measures failed. After injection of alcohol into the nerve trunk, relief followed. In some

¹ *Paris Médical*, May 27, 1916; review in *Journal of the American Medical Association*, 1916, lxxvii, 156.

cases more than one nerve trunk must be injected. All the nerve trunks tributary to the area of pain should be blocked. He employed 60 to 80 per cent. alcohol. The fear of motor disturbance need not be considered if the indications for the relief of pain are sufficiently great. Regeneration takes place within six to eight months after the alcohol injection.

He reports also some very interesting cases in which, in addition to pain, there was paralysis, and after the relief of pain following the injection, the motor function in the nerve was gradually restored. In this group there was one remarkable case of pain with median nerve paralysis. No relief after two operations. Now, after six months of pain, the alcohol injection not only relieved the pain, but rapidly restored motion.

In cases of this kind, the paralysis must have been to a certain extent partial, and, of course, the nerve was not completely severed. Sicard must be an enthusiast, as he states that there has been but one failure in 43 cases. Motor function has also returned in a large number.

There may be no relation between the use of alcohol for painful neuritis and the treatment of trifacial neuralgia, but it is interesting at this time to call attention to the splendid contribution of Byrnes¹ from the Johns Hopkins Neurological Clinic.

Beckman,² from the Mayo Clinic, reports their experience with 146 cases of trifacial neuralgia treated by the method of Lévy and Baudouin.³ Seventy-seven, of 120 cases followed, had relief from their pain for about six months or less. Beckman does not attempt to inject the ganglion itself, but only the deep branches of the nerve.

Byrnes injects the ganglion itself.

In a previous communication, Sicard⁴ used air, or a weak anesthetic, for injecting the nerve when the chief symptom was pain.

FASCIA.

The probabilities are for a number of years we shall have to turn to the monographs of Kirschner and of John Staige Davis⁵ which have been reviewed.

Mann,⁶ of Minneapolis, reports cases, chiefly hernias, in which fascia has been employed to strengthen the suture. There is no discussion of, or reference to, the literature.

¹ Johns Hopkins Hospital Bulletin, 1915, xxvi, p. 1.

² Annals of Surgery, 1916, lxiv, 244.

³ Presse Médicale, 1906, xiv, 108.

⁴ Review in Journal of the American Medical Association, 1915, lxiv, 1277.

⁵ PROGRESSIVE MEDICINE, December, 1914, p. 261.

⁶ Annals of Surgery, 1914, lx, 481.

Von Eberts and Hill¹ give their experimental work in the department of McGill University, with references to the literature, including Kirschner. Apparently this is but a confirmation of previous experiments.

Kolb² reports on the shrinkage of the fascial transplant in plastic operations upon the intestines. This is apparently a purely experimental investigation.

SKIN.

Skin-grafting. In 1909 I³ illustrated the method employed in Dr. Halsted's clinic of the Johns Hopkins Hospital. It is for large, thin Thiersch grafts.

Charles H. Mayo⁴ describes the preparation of the surface of bone for grafting. His experience and illustrations are apparently chiefly concerned with the bones of the skull, although he mentions some other bones. Fig. 49 pictures the drilling, Fig. 50 the granulation tissue growing out of the drill holes and spreading over the surrounding bone like a mushroom. I have had considerable experience with placing grafts on bone, and in the majority of cases I have used a chisel. The bone is chiseled until there is a little bleeding, the cross-cuts are made, also with the chisel, in the shape of mosquito-netting, but not as fine. The grafts are immediately placed on this fresh bone surface. The grafts usually take. The only advantage this method has over Mayo's is that it shortens the time of convalescence. One does not have to wait for the bone granulations to form.

PINCH GRAFTS. John Staige Davis⁵ gives the most recent and up-to-date description of the method devised by Reverdin in 1869. It is fully illustrated. These pinch grafts have a definite place in the surgery of chronic ulcers, and I would advise everyone interested in grafting to read Davis's article for the details. I am impressed that the Reverdin graft is becoming a lost art.

Davis⁶ also calls attention that skin-grafting can be done in the outpatient department in the ambulatory treatment of ulcers. He reports 50 cases. Apparently, the results have been as successful as when the patients were admitted to the wards. All were autografts, the majority small, of the Reverdin or pinch-graft type. Some were complete grafts, others partial in stages. The grafts were placed on clean, undisturbed granulations. Undoubtedly, Davis has made a great addition to the outpatient treatment of chronic ulcers.

¹ Surgery, Gynecology and Obstetrics, 1914, xviii, 318.

² Deutsche Ztschr. f. Chir., 1913, cxxv, 398.

³ PROGRESSIVE MEDICINE, December, 1909, p. 220.

⁴ Annals of Surgery, 1914, lx, 371.

⁵ Journal of the American Medical Association, 1914, lxiii, 985.

⁶ Ibid., 1915, lxiv, 558.

Tanner's Ulcer. Da Costa is constantly reminding us of rare conditions which we have previously overlooked. On this occasion, with Jones and Rosenberger,¹ he calls our attention to what we may look

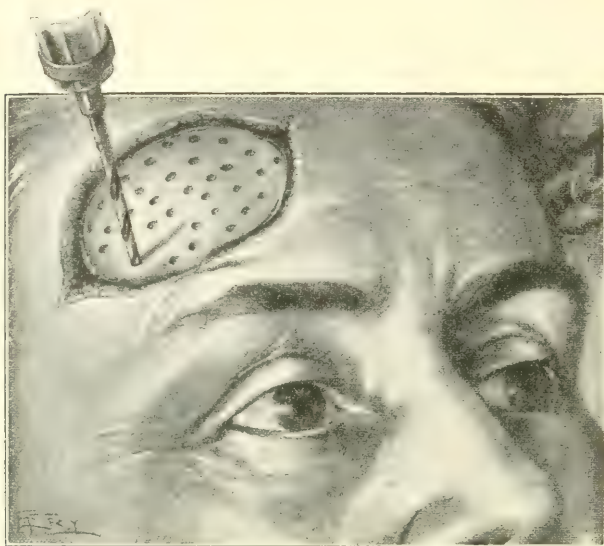


FIG. 49.—Drilling surface to diploë. (Mayo.)



FIG. 50.—Granulations appearing through outer plate for blood supply to graft. (Mayo.)

upon as an occupational ulcer. In the beginning of their paper there is a brief summary of occupational diseases. Da Costa, with Keen,

¹ *Annals of Surgery*, 1916, lxiii, 155.

became interested twenty years ago in ulcers on the hands of tanners and occasionally on the hands of cloth handlers and dyers. This ulcer has a tendency to penetrate deeply; it is intensely painful and resists all ordinary treatment. Then an opportunity came for Da Costa and his co-workers to make an intensive study of the tanner's ulcer or leather worker's ulcer. The article gives a summary of the literature of chrome sores in general. Undoubtedly there is more than one irritant substance among the etiological factors. In winter, the ulcer is worse than in summer. If the patient stops work at once, the ulcer will heal, but even then it may leave a scar. In addition to ulcers on the hands of the worker, there may be vesicles, pustules and eczema on other parts of the body due to scratching with fingers contaminated with chromium.

Fig. 51 illustrates a recent ulcer, and the amputated stump of a finger removed for a similar ulcer.



FIG. 51.—Amputation as the result of chrome ulcer eating into joint. Active chrome ulcer present now. (Da Costa.)

Da Costa has seen 44 cases, and has detailed records of 19. The length of time during which the individuals worked in chromates varied from two months to eighteen years. Seven cases—all in old workmen—showed scars of previous ulcerations. Apparently, the best treatment is prevention. When the ulcer has become chronic, the disease must be excised, often involving the loss of a finger.

Dr. Louis Levi, chief chemist of a leather company in Milwaukee, is supplying an ointment to the men to be applied twice daily. It consists of three parts petrolatum and one part lanoline.

This article of Da Costa is another indication of the new advance in preventive medicine which has to do with occupational diseases and their prevention.

One should turn to this article for the literature up to date.

Of course, there are other poisons which will produce similar ulcers on the hand or feet. Photographers, röntgenologists, and all those who

work with chemicals, especially constantly with the same chemicals, should bear this possibility in mind. Some individuals develop immunity, others are specially susceptible. Vaseline is very cheap and accessible, it can easily be rubbed into all the crevices of the skin, on the hands, fingers and about the nails, or in some cases the feet, and this may be found sufficiently protective.

I may have an opportunity to collect some recent experiences with painful ulcers of the toes, especially at the junction with the foot, which clinically and microscopically resemble chrome ulcers. My attention to these cases was called by Dr. Stewart. The cases were observed in the out-patient departments of Johns Hopkins and St. Agnes' Hospitals. The most distressing feature is the intense pain. Every known conservative treatment for the healing of these ulcers has been attempted. One patient, a motorman, had lost eighteen months in time. In all of these cases I advised the radical removal of the ulcer and a sufficient portion of toe and foot to get at tissue with good circulation. In all of the cases the patients were able to return to work. In one of the ulcers cancer has developed. Unfortunately, in this group of cases we did not investigate the etiological factor.

The question of the development of cancer in these ulcers was not considered by Da Costa. Of course we know that cancer is less likely to develop on an ulcer of the hand or foot than on the tongue, but, when the ulcer is due to some chemical irritant, and this irritation is kept up, we may have in the ulcer an atypical growth of epithelium which cannot be distinguished histologically from cancer. In 1914 I¹ reviewed such a case. The microscopic cancer was found in a tubercular ulcer at the end of the nose in a girl of eleven. The Japanese have recently produced cancer with metastases after injecting scarlet R into the skin over the abdomen in rabbits. I have recently observed an ulcer on the face which was being treated by injections of scarlet R. Clinically, there was no evidence of cancer. There had been an old scar with an ulcer in the center of it, which we had excised many years before and found no evidence of cancer. Fortunately, we had preserved tissue for restudy. I excised the recurrent ulcer with a large margin of healthy tissue down to the bone of the antrum, fearing, on account of the injections of scarlet R, that a cancer might have developed. The sections showed typical spinocellular cancer with pearly-body formation.

I emphasize this point in the relation of cancer to all chronic ulcers, to urge the profession not to tinker with any ulcer until its character has been definitely ascertained from a careful history and the microscopic study of a piece excised with the cautery.

Perforating Ulcer of the Foot. The experienced surgeon seldom sees the early stage of many of the very interesting lesions of the feet. Corns,

¹ PROGRESSIVE MEDICINE, December, 1914, p. 272.

callosities, ingrowing toe-nails, deformities of the nails, granulation-tissue tumors of the nail bed, ulcers, and—most tedious of all—the perforating ulcer, all of these come under observation late. In the past, the majority of observers have looked upon perforating ulcer of the foot as due to some primary trophic changes in the skin associated with locomotor ataxia. But Richard Levy¹ is of the opinion that the primary lesion is a neuropathic arthritis, and that the condition should be treated on this diagnosis.



FIG. 52 (Case 2).—Synovial lesion of the skin of five months' duration. The inflammatory areola is due to the use of caustics. (Sutton.)

Synovial Skin Lesion. Richard L. Sutton,² of Kansas City, reports 2 cases. Fig. 52 pictures this lesion in a female, aged fifty-eight years; the duration of the symptoms was eighteen months. Note the smooth, round, pea-sized, fluctuant tumor located over the distal phalanx of the right middle finger (in the original the illustrations are confused). This lesion had been incised and fluid evacuated on several occasions; the fluid was serous in character, or lymph. The lesion was treated with iodine, because the patient refused to stay for any longer method of treatment.

I have just excised such a tumor situated in the same place, with about the same history, only of shorter duration. It had recently ruptured and presented an umbilicated appearance. Histologically, it is a lymph cyst beneath the epidermis. I have never seen a similar condition under the microscope as a subepidermal lesion. Sutton, who gives Hyde's original description, furnishes no microscopic study, but quotes Hyde's statement that the lesion is a synovial bursa beneath the epidermis.

¹ Beitr. z. klin. Chir., 1910, lxx, 627; Mittheilungen a. d. Grenzgeb. d. Med. u. Chir., 1910, xxi, 627.

² Journal of the American Medical Association, 1916, lxvi, 565.

In the second case reported by Sutton, radium accomplished healing. The excision of tumors of this kind is such a simple affair, that I do not see why one should bother with anything else. Here we have, therefore, another finger tumor. It may also occur on other portions of the hand.

Skin Tubercle. In 1913 I¹ illustrated the gross and microscopic appearance of a butcher's tubercle. In cases of this kind there is a sub-epidermal nodule adherent to the skin. Now and then there may be ulceration, and, over the ulcer, scab formation. The butcher's tubercle is really a chronic form of tuberculosis of the skin, and the cases I have seen have been painless tumors. Owen,² of Philadelphia, describes a painful subcutaneous tubercle. The tumor apparently was well-known to the older pathologists, among them Paget. It was first described in 1812 by William Wood. Recent literature pays less attention to these tumors. They usually occur on the extremity, more often on the lower. They may occur on the body, and have been reported on the face. The painful tubercles are situated beneath the skin and are seldom attached to the skin. It has a well-defined capsule. Yet, when Owen comes to describe the structure, he says these tumors are classified as neuro-fibromas. It seems to me to be a mistake to call a connective-tissue tumor a tubercle. The tubercle should be confined to an area of tuberculosis appearing clinically as a localized tumor. It was natural for the older pathologists to confuse the butcher's tubercle with the neuro-fibroma.

This painful tubercle described by Owen is really a very common skin tumor, but it is rarely, if ever, seen on the skin of the hands or fingers. It is often multiple. I have considered these tumors most fully in *PROGRESSIVE MEDICINE*, December, 1903, p. 158. Not all painful subcutaneous nodules are fibroma molluscum of von Recklinghausen. Almost any connective-tissue, or epithelial, tumor appearing as a subcutaneous nodule may be painful. I trust the term "painful tubercle" will be dropped.

Blastomycetic Dermatitis. In 1907, I³ reported a case of cancer in blastomycetic dermatitis, and referred to this case in 1914⁴ and also again reproduced the illustration, because I do not now believe that it was carcinoma. Of course, it would be possible to cure an early cancer by a local excision, but the patient had had a similar lesion elsewhere which had healed spontaneously. It is another example of atypical growth of epithelium excited by an inflammatory lesion. I have frequently referred to these. The patient is well now, ten years since operation. The microscopic sections have been frequently restudied and compared with sections of other cases, but in this one there is present more atypical

¹ *PROGRESSIVE MEDICINE*, December, 1913, p. 242.

² *Annals of Surgery*, 1915, lxi, 451.

³ *PROGRESSIVE MEDICINE*, December, 1907, p. 199.

⁴ *Ibid.*, December, 1914, p. 271.

growth and more areas suggesting cancer of the skin than in any of the other cases.

The case reported by McKenty and Morgan¹ also shows this proliferation of the epithelium and atypical, pearly-body formation (Fig. 53). The authors believe in the excision of the lesion if it is possible. I agree with them. I have recently seen, at Johns Hopkins Hospital, a very extensive case in which I attempted to save the limb by the complete excision of the disease, but this, and all other measures to check the disease, failed, and later the limb had to be amputated. In this case it would have been possible to resort to excision at a much earlier period, but precious time was lost with vaccine treatment and other non-operative measures.

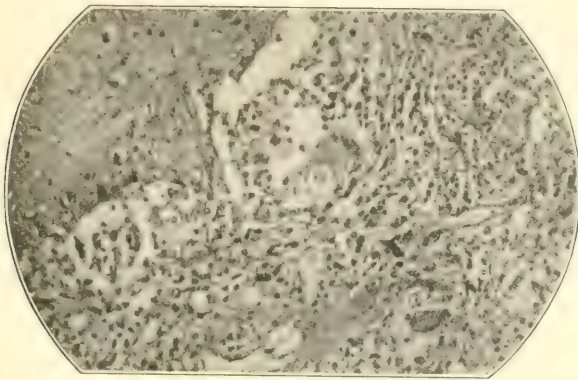


FIG. 53.—Organism situated near giant cell. Note proliferation of epithelium and atypical pearl formation. (McKenty and Morgan.)

Urticaria. I never dared to discuss the literature on this uncomfortable skin lesion, but if one is interested in the literature, a list of articles will be found in the *Journal of the American Medical Association*, 1915, lxy, 46. The first article, in 1907, suggests *x*-ray for urticaria pigmentosa; then there is an article discussing the relation of this condition to the function of the thyroid gland. Urticaria apparently may be caused by sun rays. One author claims quinine is effectual, another recommends epinephrin. Then there is discussed the occurrence of urticaria with purpura and angioneurotic edema. Another authority claims that calcium lactate is useful. Then comes the study of Solomon on the dietetic treatment of urticaria, and the last contribution is on human serum in urticaria.

Quite recently different types of food have been prepared so they can be administered hypodermically, and skin tests, similar to von Pirquet's tuberculin test, studied.

¹ *Annals of Surgery*, 1915, lxi, 513.

MUSCLES.

I¹ began the critical discussion of the literature on myositis and other lesions of the muscles in 1912 by calling attention to an example of gonorrheal myositis reported by Ware and confirmed by bacteriological study. The muscle was edematous and friable, with a definite polymorphonuclear leukocyte infiltration. I have seen no reference to this condition since.

In 1903 I² covered the literature of muscle lesions. In 1908 the literature was again reviewed.³ In 1910 there were reported⁴ some new observations of myositis ossificans. In 1912 the literature was again covered⁵ with special reference to luetic myositis. In 1913 chief attention was devoted to Volkmann's contraction.⁶ In 1914 the rare condition myositis ossificans progressiva only was considered.⁷

As I glance back over this literature and compare it with my own experience, I am impressed with the following facts, which, I think, should be borne in mind:

In the vast majority of cases of fracture or when patients' extremities require some fixation dressing, or when the individual must be confined to bed, all the attendants, from the chief down, neglect efforts to maintain muscle tone by encouraging active motion, by introducing passive motion, by massage, by some form of electricity, and by baths.

The neglect of the muscle undoubtedly increases the period of disability, and when added to this neglect there has been injury due to tight dressings, we may have a chronic myositis of the ischemic type, leading to various degrees of deformity and disability.

In the second place, when either tubercular or syphilitic myositis is a single lesion, we may experience great difficulty in differentiating it from sarcoma. In some cases of syphilis, the Wassermann reaction may be negative. In a number of cases of tuberculosis it may require a number of sections before the typical giant cell and tubercle is found. In two cases in which tissue was sent to me for diagnosis, my first impression was sarcoma, which, if I had allowed it to go unchecked, would have led to the amputation of two useful limbs. In one case the administration of salvarsan, notwithstanding a negative Wassermann and in spite of sections suggesting sarcoma, cleared up the diagnosis of syphilis. In the second case, after many sections were cut, typical tubercles and giant cells were finally found. The present condition of these patients confirms the diagnosis of benign myositis.

The majority of surgeons are beginning to think of ossifying myositis as a not infrequent result of muscle contusion, to recognize it in the

¹ PROGRESSIVE MEDICINE, December, 1902, p. 137.

² Ibid., December, 1903, p. 178.

⁴ Ibid., December, 1910, p. 220.

⁶ Ibid., December, 1913, p. 252.

³ Ibid., December, 1908, p. 167.

⁵ Ibid., December, 1912, p. 276.

⁷ Ibid., December, 1914, p. 253.

x-rays by bone shadows in the muscles, and not to subject such patients to operation in the bone-forming stage, because experience has taught us that an operation then simply makes matters worse.

Both surgeons and pathologists are learning to differentiate the succulent granulation tissue, with its bone islands of ossifying myositis, from sarcoma.

From my personal investigation, I have been unable to confirm the opinion of some authors that sarcoma develops in ossifying myositis. As far as I can make out, sarcoma and myositis ossificans are the results of trauma to muscle. In one instance the granulation tissue develops into sarcoma; in the other there is ossification, but, after ossification, sarcoma can be practically excluded. This is not necessarily true of ossifying periostitis, but whether it is true or not, it is impossible to differentiate the lesions, because after a trauma to bone, new bone formation takes place in both conditions—the benign periostitis and the periosteal sarcoma.

Muscle Hematoma. J. Lambrethsen¹ reports a spontaneous rupture of the rectus muscle during a fit of coughing, with the development of a tumor due to hemorrhage. The abdominal symptoms suggestive of some intra-abdominal condition were relieved by removing the blood from the cavity between the torn muscles. The surgeon was led to explore there by the palpation of a tumor. This patient had previously had a rectus incision for a cholecystectomy ten years before. There had been a fistula from the cystic duct for four years. Such a condition would probably have been associated with myositis of the muscle. However, in my experience with reoperation through old rectus scars, I have been surprised at the almost normal appearance of the muscle in cases in which the suture had been good and there had been healing *per primam*. Even microscopic studies about pieces of silk, removed with the surrounding muscle at the second operation, have shown very little reaction. For this reason surgeons need not fear spontaneous rupture with hematoma as a frequent postoperative complication. Nevertheless, it is a thing to be thought of in scars which suddenly become painful, and in which areas can be palpated.

I have operated once for a hematoma infiltrating the entire right rectus muscle. The patient was an alcoholic, had cirrhosis of the liver and was kicked on the abdomen. There were immediate abdominal symptoms, a rapidly developing tumor, great tenderness and muscle spasm. In view of the strength of the rectus sheath, one got the impression, from the history and a careful examination, that it was an intra-abdominal condition. Even when I had exposed the right rectus, turned out blood clots, and examined the muscle infiltrated with blood, I was not convinced that it explained the symptoms. For this reason

¹ Review in Journal of the American Medical Association, 1915, lxy, 370.

the abdomen was explored and the cirrhotic liver exposed. This patient recovered and has remained well since.

The most common form of hematoma is in the sterno-cleido-mastoid muscle in children after birth. The most frequent form of hematoma later in life I believe occurs in the psoas and iliacus muscle, usually in children, but now and then in adults. There may be an interval of time between the injury and the symptoms. The clinical picture suggests arthritis of the hip, or, in later stages, psoas or iliopsoas abscess. In my cases, the x-ray has shown no bone lesion, nor has the hematoma appeared in the x-ray plate. As a rule these cases are operated on when the hematoma has become infected. There is no indication to operate unless there are signs of infection. In my most recent observation, the adult woman was most carefully studied in the wards at St. Agnes' Hospital and was referred to me with the diagnosis of perithelial angiosarcoma of the pelvis. The only fact in favor of hematoma was the absence of any bone destruction which should have taken place even if this malignant tumor had been primary in the intermuscular fascia. Even when the tumor was explored, sarcoma could not be excluded, because, as I will describe, there is a hemorrhagic cystic sarcoma. But at the bottom of the cavity there was purulent material which I have never seen in a sarcoma. I was so certain of my diagnosis that I did not take a piece of the wall for microscopic section. I know now that I missed an opportunity to study muscle outside of a slightly infected hematoma. The wound in this case healed so readily that malignant disease can be excluded.

Muscle Rupture. Emory G. Alexander,¹ of Philadelphia, reports, with illustrations and complete literature, rupture of the biceps flexor cubiti. In case I the ruptured muscle was sutured. In Case II there was an old rupture of the tendon of the long head of the biceps with fibrous union to the belly of the muscle; the scar was excised, the tendon split, and the muscle sutured between the split.

In Case I the rupture was a recent one, and the patient was immediately subjected to operation. The wound healed *per primam*, but there was marked atrophy of the muscle and recovery was slow. It is noted that massage and electric treatment were given and that the patient—a laborer—was able to return to his occupation, but the late result is not known.

In Case II the history of an injury dated back four years, with immediate signs of rupture of the biceps; there was no operative treatment, and since this injury the patient has been unable to return to his former work.

These two cases should be contrasted. Both were seen by physicians: One was immediately diagnosed and properly treated; the other was

¹ Annals of Surgery, 1915, lxi, 608.

incapacitated for four years, until relieved by proper surgery. Cases of this kind should be collected by those interested in the development of industrial surgery and medicine.

It may not always be necessary to operate on a case of ruptured muscle or aponeurosis. It is difficult during the first few days to distinguish the complete, from the incomplete, rupture. Gerster (quoted by Alexander) has reported a case successfully treated with a sling. I have two cases not operated upon, seen and recognized in the recent state, which have healed with full restoration of function and with but a brief period of disability. From these cases I have concluded that it might be wiser to wait if there is no other urgent indication for operation. During such an interval, we have an opportunity to distinguish the cases in which operation is not necessary.

Then, again, I am rather of the opinion, although I have not the facts to prove it, that a few days to give the tissues a chance to recover from the trauma and to establish collateral circulation, might be helpful in shortening the period of disability. It seems to me that in Alexander's first case the atrophy of the biceps after immediate suture was greater than if the muscle had been sutured four or five days later. This very important point was apparently not investigated by Alexander, nor apparently by any of the others. The conclusion that operative treatment is to be recommended is by no means all we want to know. The next most important point is, when to operate and what other measures will shorten the period of disability and prevent the temporary muscle atrophy.

HÜTER'S SIGN. According to Alexander, Hüter calls attention to the fact that flexion of the forearm in pronation when the biceps is tense is more forcible than when the forearm is supinated and the biceps is relaxed. Apparently, this sign was not present in many cases. I am trying to practise it on my own arm now and it does not impress me as a sign that would be particularly helpful in differentiation, and apparently the majority of surgeons have operated whether it was present or not.

One can be assured that rupture of a muscle or tendon can and should be recognized after the injury, and with such recognition, followed by proper treatment, the great majority of individuals should be able to return to their former occupation, without loss of efficiency.

In 1912 ¹ reported the experiments of Caminiti which showed that we cannot expect much muscle regeneration after an injury. If there are large gaps, the defect will be filled by granulation tissue, and only the contraction of this tissue will bring the muscle ends nearer together—another argument in favor of operation.

The entire subject of rupture of muscle and hernia has previously been discussed.² Practically all the literature in Alexander's article has

¹ PROGRESSIVE MEDICINE, December, 1912, p. 277.

² Ibid., December, 1908, p. 169, and December, 1912, p. 277.

been mentioned by me, and I wrote in 1908, from the review of the literature up to that date, that equally good results have been accomplished by rest, fixation, and massage. The indication for operation is governed by the size of the defect and the extent of function lost. I would add here that in all cases it might be well to wait a few days before operating.

I have the impression that the majority of surgeons use catgut, probably chromic. I am inclined to think that a more perfect suture, if there is not too much tension, can be best obtained by fine sutures with interrupted silk. I base this upon the wonderful functional results I have observed after division and suture of the thyroid muscles and the sternocleido-mastoid in lobectomy for goitre, and the observation just mentioned of the almost normal appearance of muscle about such buried silk sutures.

Myalgia. We frequently observe pain in the region of muscles after contusion, strain, or overexertion. The pain and tenderness may be extreme; sometimes there is a palpable knot in the muscle (Charlie-horse). One rarely, if ever, gets an opportunity to examine the muscle in such cases. On three occasions, I have explored the lateral abdominal muscles on the left side for persisting local pain and tenderness after injury. Microscopically, nothing could be made out. For reasons difficult to understand, the patients were relieved by the operation. It is a not infrequent occurrence in the pectoralis major muscle, especially in individuals who begin to play golf late in life. When the patients are women, we have to exclude a breast lesion.

R. Le Fort¹ reports an observation which he looked upon as painful myositis and neuritis after a contusion. Apparently, there was no question as to the reality of the pain. The contusion of the leg after a bomb explosion was followed immediately by swelling, but the chief symptom was intense pain in the limb, not localized. The muscles atrophied and "two large bunches could be palpated in the leg." Le Fort explored the popliteal space; found the popliteal artery contracted and without perceptible pulsation. The artery was stripped for a considerable distance. The relief from pain was complete in five days.

From this description one would feel that there was some interference with circulation, somewhat of the same type as in Raynaud's disease. Although I feel that Le Fort has not given us all the facts which would lead us to agree with his diagnosis of myositis and neuritis, yet he has illustrated a not unusual condition following injury. It is true that the majority of these cases yield to non-operative treatment, but in those in which the treatment fails, operation should be considered. The painful muscle is explored, the nerve isolated if found surrounded by scar tissue, and the larger vessel supplying this area examined, and, if they are in the

¹ Bull. de l'Acad. de Méd., May 16, 1916; review in Journal of the American Medical Association, 1916, lxxvii, 79.

condition described by Le Fort, stripped. One should also look for varicose or thrombosed veins.

Luetic Myositis. I wish to call attention again to my review¹ of Landois's article in which he dwells upon the importance of giant cells as the chief histological evidence of a syphilitic myositis. In my limited experience, I have been unable to confirm this.

Volkman's Contraction. This name separates this form of ischemic myositis from other forms of myositis, because the contraction represents the chief clinical sign and the complication demanding relief.² The first case of Volkman's contraction which came under my observation seventeen years ago is now about twenty-seven years of age. This otherwise normal individual has been tremendously handicapped. He is now demonstrating and selling dictaphones. The original injury was a simple Colles's fracture. At that time there was considerable enthusiasm in favor of the immediate fixation of all fractures in plaster of Paris. This boy had his dressing on one week. He came under my observation about six months later, and I have operated at least ten times. The contraction is not completely relieved; there has been a great deal of retardation of growth of bone, the length of all the bones of the forearm, hand and fingers, is affected. In my operations, I isolated every nerve and vessel and every fibrous muscle, lengthened and transplanted tendon. These operations were done before the advent of the use of fascia or fat transplantation.

Cases of this kind should be constantly brought up in the literature to act as a warning against the employment of all tight fixation dressings immediately after injury. Apparently, if the dressing remains on but twenty-four hours, the harm is done; the myositis has begun, the contractions will follow.

John B. Murphy³ remarks that of the three possible forms of pressure—effusion or hemorrhage, flexion, and the splint—the most common cause is the splint.

Personally, I have never seen, nor read of, a marked case of Volkman contraction in which the limb—usually the forearm—had not been placed in a splint.

Ossifying Myositis. This subject has been so fully covered in past reviews that I shall attempt to note with the more recent literature only those things that appear to be new observations or old points to be re-emphasized.

Oliver J. Fay,⁴ of Des Moines, had an unusual experience with six cases in ten months. In his article there are excellent photomicrographs, of which Fig. 54 is a good example. However, this is not the stage in

¹ PROGRESSIVE MEDICINE, December, 1912, p. 279.

² Ibid., December, 1913, p. 254.

³ Journal of the American Medical Association, 1914, lxiii, 1249.

⁴ Surgery, Gynecology and Obstetrics, 1914, xix, 174.

which there is any difficulty in histological diagnosis. It is in the cases in which the lesion of the muscle is explored before bone formation that we wish to be familiar with this peculiar granulation tissue, in order to distinguish it from sarcoma. When the lesion extends to the bone,

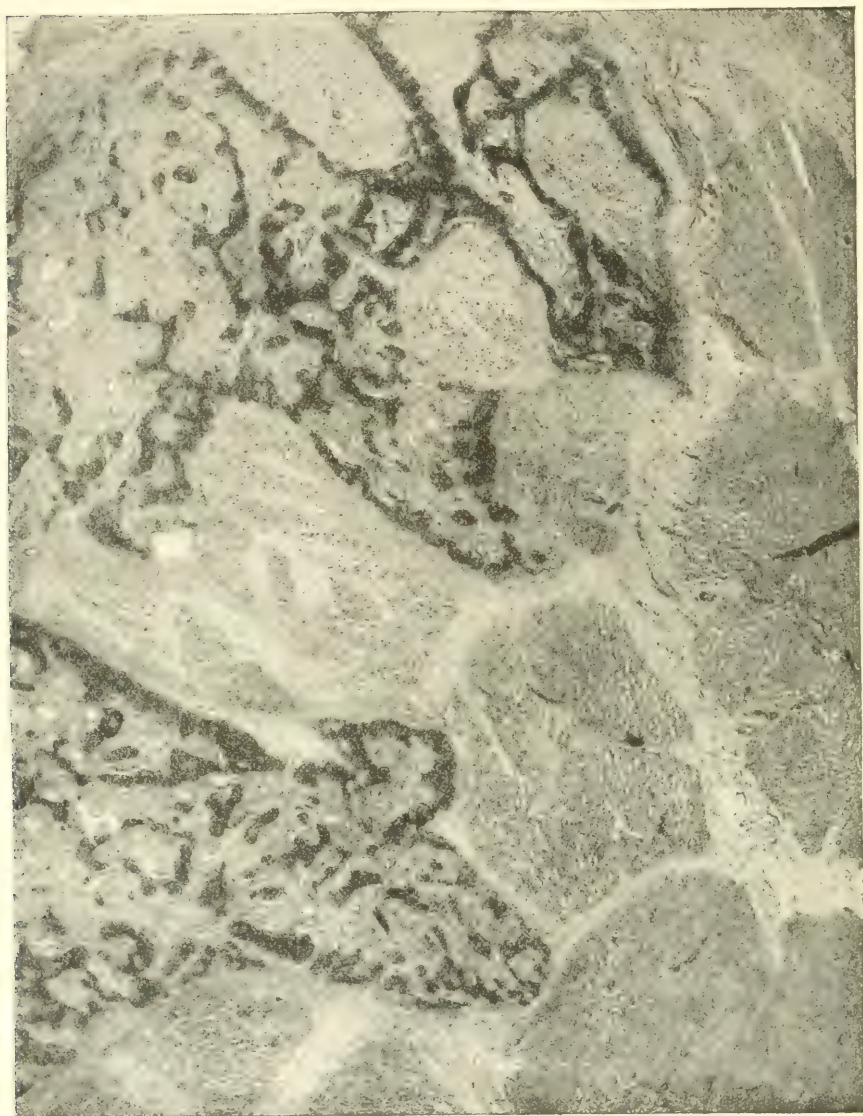


FIG. 54.—Showing the intimate relation of muscle and bone. (Fay.)

bone formation is not helpful in distinguishing it from periosteal sarcoma. To the present time, no one has published histological pictures of this kind. Fay's article contains about forty-three references to the literature.

Paul Oliver,¹ of Chicago, reports two interesting cases involving the elbow-joint following a single trauma. The most common position for this ossifying myositis is in the rectus muscle after a single contusion, and about the elbow-joint after dislocation with, and without, fracture. From my investigation, the thigh cases are pure ossifying myositis, while in many of the elbow cases it is easier to explain the bone formation as of periosteal origin.

S. Goto,² from a study of five human cases and experiments on rabbits, is of the opinion that the bone forms spontaneously in the muscle or from nearby periosteum, and in some cases from both. He suggests that early intervention, with evacuation of the hematoma might prevent bone formation, but furnishes no cases to prove this.

Goto is inclined to think that bone begins to form at the end of a week and urgently advises against massage, but recommends heat and baths. Operative measures are not indicated until all the local reactions have subsided, and when the x-ray shows no evidence of retrogression.

Shere³ takes up the question of the differential diagnosis between myositis ossificans and traumatic sarcoma. In both lesions, there is an unusual local reaction to the ordinary trauma. The local lesion may be intermuscular or periosteal. He quotes Coley and Finney, but this is older literature, when we knew less about ossifying myositis and not much more about sarcoma. Shere reproduces an excellent photograph (Fig. 55) which was diagnosed by Murphy as periosteal sarcoma, as shown in the histological section (Fig. 56). I hope to have an opportunity to show an x-ray of a lesion of the femur not unlike that shown in Fig. 55 which proved to be an ossifying periostitis and not a sarcoma. Although Coley is of the opinion that sarcoma has developed in ossifying myositis, I have never been able to read the evidence that way. I cannot follow Shere's reasoning in the relation between sarcoma and myositis. Apparently, he is of the opinion that these cases should be opened and drained at once. Ossifying myositis always follows a subcutaneous wound. If the wound is opened at once, bone formation and perhaps sarcoma might be prevented. This is a very interesting suggestion. At the present time we know of no means of prevention, and, with few exceptions, none of the previous investigators have considered prevention. I have just mentioned that Goto recommends the evacuation of the hematoma when it is recognized.

Dean Lewis, of Chicago, when discussing Shere's paper, is of the opinion that there is no relationship between myositis ossificans and sarcoma. Lewis also favors delay in the operative treatment of the myositis ossificans. McGlannan, who discussed the paper, also advised against immediate operation. No one, therefore, seemed to agree with Shere,

¹ Journal of the American Medical Association, 1915, lxiii, 1453.

² Review in Journal of the American Medical Association, 1915, lxiv, 783.

³ Journal of the American Medical Association, 1915, lxv, 1012.

but I am very much impressed with what he has to say about early operative intervention. That is, before the *x*-ray shows bone formation, in the stage when we feel the induration, it certainly could do no harm;

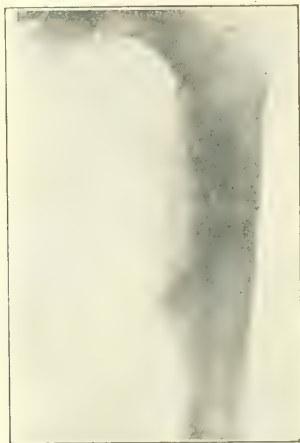


FIG. 55.—Mixed, round- and spindle-cell periosteal sarcoma of the right femur having its origin on the inner side of the femur and extending into the adductor group of muscles. Anteroposterior röntgenogram made before operation. Note the radiating columns of bone sticking straight out from the femur through the tumor-like thick bristles. A röntgenologic feature characteristic of periosteal sarcoma. (From Clinics of John B. Murphy, February, 1915.) Compare with Figure 1. (Shere.)

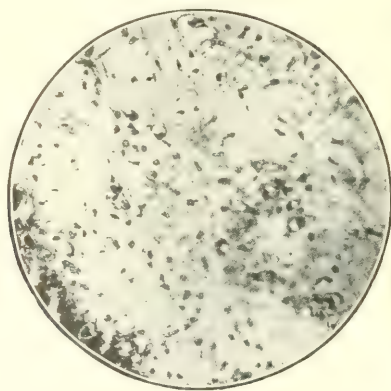


FIG. 56.—Mixed, round- and spindle-cell periosteal sarcoma of the femur. This area shows cartilaginous metaplasia with calcium deposit at the extreme edge. (From Clinics of John B. Murphy, February, 1915.) Compare with Figs. 2, 3, and 4. (Shere.)

we might learn that it does prevent bone formation, and also, it is possible, that a sarcoma in some cases would be recognized to the great benefit of the patient.

Shere, therefore, offers undoubtedly a new point of view, toward which we have no right to be antagonistic. As a matter of fact, we are making but little progress in the early recognition of these traumatic sarcomas, and none in the prevention or satisfactory treatment of myositis ossificans.

TENDONS.

I think it wise to briefly review some of the rarer conditions which bear relations to tendons and which have been discussed here in the past. I find that my colleagues rarely think of these exceptional possibilities, and, to keep them in mind, we must be constantly testing the communications between our association centres.

Snapping shoulder,¹ jerking finger,² and snapping hip³ may come under our observation only once or twice in a lifetime, and it will be most satisfactory to be able to turn quickly to the scanty literature.

Hematoma of the tendon sheath⁴ seldom occurs. The probabilities are that the hemorrhage within the tendon sheath has no relation to the osteoid tumors outside the sheath which I will discuss later. But hemorrhage may act as a foreign body, and organization of a hematoma is not uncommon. I have just examined such a case under the microscope. The patient had received a contusion on the temporal fossa with immediate development of a little tumor which, after a few days, became slightly smaller, but has remained as a subcutaneous nodule. It appeared like a compact mass of powder in the subcutaneous tissue. Under the microscope, it was composed of branching lines of blood-pigment encased in fibrous tissue. That is, the blood as a whole was not encapsulated, but apparently at one time the entire blood-clot had become permeated with vascular granulation tissue which later changed into scar tissue and now nothing remained of the blood, except the pigment encased in scar tissue.

It is difficult to imagine, in the various sprains and other injuries of the extremities, that blood does not often enter the sheath and may later give rise to some form of chronic synovitis. A special disease of the tendo Achillis has been described⁵ in which there is considerable thickening of the tendon after a trauma.

Then there may be ossification of the tendon.⁶

Then we have the rare stenosing fibrous tenosynovitis⁷ which must not be confused with tenosynovitis crepitans.

Infection of the Tendons of the Hand. As Kanavel's excellent book is out of print, I wish again to refer to the original article⁸ on which the

¹ PROGRESSIVE MEDICINE, December, 1914, p. 255.

² Ibid., December, 1912, p. 260.

⁴ Ibid., p. 289.

⁶ Ibid., p. 296, and December, 1913, p. 267.

⁸ Surgery, Gynecology and Obstetrics, 1909, viii, 49, 125.

³ Ibid., p. 294

⁵ Ibid., p. 291.

⁷ Ibid., p. 267.

book was based. It is fully illustrated, and one who is called upon to treat infections of the fingers and hands should go over these articles most carefully.

In the past few years circumstances have allowed me, through my younger associates at St. Agnes Hospital, to see a large number of infections of the hand, and I know of no work which has helped me more in directing these young surgeons as to the proper incisions for drainage.

Wounds of Tendons. When there is a wound of the hand or fingers, one cannot be certain that the tendon is not involved. Loss of function suggests involvement, but this possibility should always be borne in mind, and for this reason the immediate and primary treatment of such a wound is the chief factor in the protection against the infection which, if a tendon is involved, prolongs the convalescence and often increases the disability.

Now that the employer, through the workmen's compensation act, must pay the bill, more interest is being taken in these apparently simple wounds.

The letter from George M. Dorrance,¹ of Philadelphia, to the editor of the *Journal of the American Medical Association* calls attention to the fact that a large number of fingers have been amputated because of secondary infections.

He admits that in some cases the infection is primary, but that, in perhaps a larger percentage, the infection is due to improper handling of these simple wounds.

I agree with Dorrance that the best environment for the treatment of such wounds is a modern operating room in a hospital or dispensary. The physician or surgeon who handles such a wound should put on gloves and prepare as for a major operation.

Even in our best hospitals and in the clean environment of the outpatient clinic, it is difficult to get younger surgeons to feel the responsibility of taking such precautions in these simple wounds. How much more should they be criticized for this neglect when everything else about them is surgically clean, than the general practitioner who is called upon to treat such cases in his office, or in the shops.

If we succeed in teaching the public how to cover such a wound with a sterile piece of gauze from a first-aid package, and then to come at once to a surgeon, we will be able to force the surgeon to be clean. At the present time, if the wound suppurates and the tendon is infected, it is very easy to blame the infection on the improper handling of the wound in the first instance before the surgeon saw it.

From my recent experience, I am confident that Dorrance is right, especially as to tendon infection. It is primary, as often as it is due to a lack of special care by the surgeon in the treatment of the wound.

¹ Journal of the American Medical Association, 1916, lxvi, 1734.

Iodine will *not* protect against dirty hands; gloves *must* be worn in this as in all other forms of operative surgery.

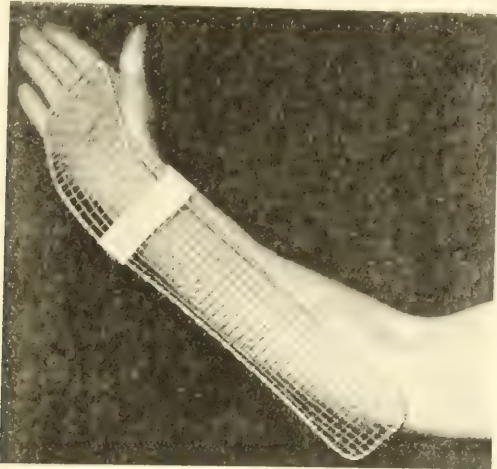


FIG. 57.—Adjustable wire splint for drop wrist. (Lyle.)



FIG. 58.—Tuffier splint. (Lyle.)

James H. Kenyon,¹ in describing the suture of tendons and nerves after wounds of the wrist, pictures two excellent splints (Figs. 57 and 58). Tuffier's splint was devised to hold the hand when there was wrist drop after paralysis of the musculospiral nerve, and, until this paralysis is corrected, the hand should be fixed in a normal position. The abnormal position due to the paralysis overstretches the muscle and leads to degeneration and loss of function. Therefore, in addition to cleanliness, which insures the healing of the wound, we must not forget the physiological splint which protects until voluntary function is restored.

Transplantation of Tendons. Leo Mayer² writes a monographic article from a children's hospital in Berlin. In the first portion, he summarizes the history of the development of tendon transplantation, and then discusses the anatomical and physiological problems, with numerous illustrations. His research began in the clinic of Lange, in Munich, in 1912. Apparently, it was an attempt to perfect the technic of Biesalski's operation, and the latter was evidently interested in Mayer's work.

In referring to the review of the original of Biesalski's³ work in 1910, I find that he was interested in preventing adhesions between the transplanted tendon and the surrounding tissues. He has two methods: One, to surround the transplanted tendon with prepared fish bladder, and the other—preferred—method, to remove the diseased or paralyzed tendon from its sheath and introduce the new tendon into the old sheath.

This method, therefore, has been in the literature for six years. In glancing over a few of the larger recent articles, I find no reference to Biesalski's work.

Kirschner,⁴ in his large work on transplantation of fascia to replace tendons or their sheaths, does not refer to Biesalski's fish-bladder.

Rehn,⁵ in his study of free transplantation on tendons, prefers the autoplasmic method to any silk or foreign material. He does not mention Biesalski's method for preventing adhesions. Siever, Lexer and Schepelmann⁶ apparently also overlooked this method. Schepelmann uses a piece of vein to bridge the defect in a tendon instead of tendon or fascia.

I have previously discussed a contribution of Leo Mayer on this same question.

When there is a sheath, the problem is a simple one. The question is what to do when there is no sheath.

Often, when experienced operators disagree, their good results by

¹ *Annals of Surgery*, 1916, lxiii, 119.

² *Surgery, Gynecology and Obstetrics*, 1916, xxii, 182, 298 and 473.

³ *Centralbl. f. Chir.*, 1910, xxxvii, 1653.

⁴ *PROGRESSIVE MEDICINE*, December, 1914, p. 261.

⁵ *Ibid.*, December, 1914, p. 258.

⁶ *Ibid.*, December, 1913, p. 268.

⁷ *Ibid.*, December, 1914, p. 260.

different methods are dependent more upon attention to details, and the failure of one surgeon with one method and success with another can often be more easily explained by the surgeon than by the method.

Mayer brings out the fact that Lange and Vulpius, both with large clinical experience, radically oppose each other as to technic. Lange believes in periosteal implantation of the transplanted tendon, first advocated by Drobnik, and the lengthening of the tendon with silk, while Vulpius sews the transplanted tendon to the paralyzed tendon, a method first introduced by Nikoladoni. Lange sutures purposely under tension, Vulpius under slight tension, Stoffel under no tension. Lange draws the tendons through the fatty subcutaneous tissue, Vulpius beneath the fascia. There is disagreement in regard to the time for active and passive motion.

I submit to my readers who do tendon transplantation that those points on which these experienced men disagree, are quite unessential.

Mayer, however, in his problem is interested in the restoration of the normal relation between the tendon and its sheath.

In the second part of his monograph he describes three typical physiological tendon transplantations. In the third part, also profusely illustrated, he reports on some experimental and clinical results.

Mayer feels quite certain that he has confirmed the work of Biesalski on the importance of the utilization of the old sheath to allow the best function. In the last sentence of the last article, Mayer, in my opinion, makes the most important statement in regard to the success of tendon transplantation. The surgeon must be the absolute master of tendon anatomy.

One may refer to this article (p. 479) for the most complete bibliography up to 1916.

Kanavel,¹ of Chicago, presented his paper before the American Surgical Association in May, 1916. He gives his results after the transplantation of free flaps of fat to correct and prevent adhesions and contractions about tendons as well as nerves, bloodvessels, and joints. His clinical experience embraces 32 patients up to 1916. The longest period after operation was about five years. It is a purely personal report, with practically no discussion of the literature. There are numerous illustrations which have to do with the pictures of the condition before and after operation.

Among the 32 cases there were only 4 in which the fat transplant was lost due to infection. In some of the cases, fat was transplanted into infected areas. He is of the opinion that the fat lives and does not act as a foreign body. His chief experience was with tendons and joints. Fat transplants have not been successful in wounds left open, such as after breast operations and in osteomyelitis.

¹ Surgery, Gynecology and Obstetrics, 1916, xxiii, 163.

I¹ have previously reviewed the technic of fat transplantation. It originated with Makkas in 1912. From my personal experience with it, I have found it an excellent tissue to fill cavities and surround tendons.

Tendon-sheath Tumors. In 1903, when I introduced the subject of Connective-tissue Tumors, Benign and Malignant, I² described 7 cases of solid tumors, more or less encapsulated, removed from the tendon sheaths. At that time, 6 were called fibrosarcoma and 1 fibroma. I wrote at that time: "I must confess that there appears to be almost as much justification to consider all of them as innocent tumors." In every case there has been no recurrence since the removal of the tumor, and it is thirteen years since the above was written. Of these 6 cases, histologically, 1 was a pure fibroma with areas of hemorrhage, 1 was a pure spindle-cell tumor; 3 were fibro-spindle-cell tumors; 2 were fibro-spindle-cell tumors with numerous giant cells. I have restudied these cases and have not changed the histological description. Two out of 6, therefore, contained giant cells. Five of the tumors were situated on the flexor tendons of the fingers, one on the extensor tendon of the finger, and one on the flexor tendon of the plantar surface of the foot.

In 1905 I³ referred to Müller's report from von Bergmann's clinic in Berlin. Among 16 cases, 6 were classed as fibrosarcoma; 2 lipomas, 5 ganglions, 2 foreign bodies, and 1 a subungual perithelioma. I have been looking for a tumor of the last type since, but have never found one. The presence of giant cells in the fibrosarcoma of the tendon sheaths was observed by Müller in many of his cases. All of his tumors contained spindle cells, blood pigment and blood. Müller was able to follow all of his patients, and none of the tumors recurred.

In the same number of *PROGRESSIVE MEDICINE* I reproduced a photograph from an observation of my own and the painting from the gross appearance of this tumor (Plate III, opposite page 266); the legend by some mistake is incorrect, it should not be fibroadenoma of the skin. No giant cells were found in this tumor.

In 1909 I⁴ reviewed and pictured the remarkable observation of Fritsch—2 cases of diffuse giant-cell sarcomas of tendon sheaths. The diffuseness of the newgrowth would make one think of tuberculosis. I have never been able to find cases similar to Fritsch's, either in the older or in more recent literature. I am impressed with the fact that Fritsch's cases may be angiomas in which there has been increase of fibrous tissue, hemorrhage, and foreign-body giant cells.

Since 1903, as my experience with these tendon-sheath tumors has grown, I have become impressed with their benignity and have been most interested in a small group containing giant cells. Some of them

¹ *PROGRESSIVE MEDICINE*, December, 1914, p. 294.

² *Ibid.*, December, 1903, p. 171.

³ *Ibid.*, December, 1905, p. 262.

⁴ *Ibid.*, December, 1909, p. 204.

are not unlike the fibrohemangiomas which I¹ described in 1903. We now know that some of these tumors contain cholesterol and are called *xanthoma*. These giant-cell fibromatous tumors of the tendon sheaths, the giant-cell epulis of the jaw, the giant-cell tumor of bone, the fibrohemangiomas of tendon sheaths (*xanthoma*), are a very interesting group of tumors.

The most thorough of the recent contributions to tumors of the tendon sheaths is by Stewart and Flint,² of Leeds.

I will review later Stewart's extensive contribution to giant-cell tumors of bone. He there uses the term myeloid. When describing the giant-cell fibroma of the tendon sheath, he employs the term myeloid tumor of the tendon sheath.

The first case of non-osseous myeloid tumor was described by Broca. In 1913 Tourneux was able to collect 45 examples from the literature. Stewart and Flint bring the total of reported cases up to 73. The first English report is by Targett in 1897, under the title "Giant-cell Tumors of the Integument." I am sorry that the Transactions of the Pathological Society of London have such a limited circulation. If the reverse had been true, the term giant-cell tumor might have found its fixed and proper place in tumor terminology and supplanted giant-cell sarcoma, myeloid, and myeloma.

When I introduced the subject in 1903 and described the presence of giant cells in these tendon-sheath tumors, I unfortunately did not get hold of Targett's article, nor of Bellamy's in 1901; nor did Müller. Stewart calls attention to the various views in regard to these peculiar giant cell tendon-sheath tumors. Targett, in 1897, looked upon them as spindle-cell sarcoma and could not explain the presence of giant cells, nevertheless he called them giant-cell tumors. It was not until 1913 that Fleissig advanced the view that these tumors were granulation-tissue tumors and not true neoplasms. *Xanthoma* cells were found in the giant-cell tumors of tendon sheaths in 1898 by Dor.

Stewart and Flint then report their two cases in detail. Fig. 59 is a sketch of the location of the tumor near the scar of an old injury; Fig. 60 shows the microscopic picture—giant cells in endotheliomatous tissue. In their second case they reproduce a microscopic drawing of the *xanthoma* or foam cells (Fig. 61).

One will find in this article the best description of the cholesterol found in these tumors, as it was present in considerable amount in their second case.

Stewart and Flint conclude that these myeloid tumors of tendon sheaths are relatively benign and can be treated conservatively. Even when they recur, second local operations should be tried. They write: "The

¹ PROGRESSIVE MEDICINE, December, 1903, p. 154, Fig. 17.

² British Journal of Surgery, 1915, iii, 90.

tumors can usually be shelled out." Personally, I object to this method with any tumor, and I know from personal experience that these tumors of the tendon sheaths can be dissected out without injury to the tendon. As Stewart and Flint correctly state, this giant-cell tumor may arise from fascia as well as from the tendon sheath.

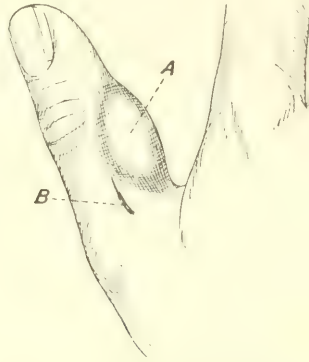


FIG. 59.—(Stewart and Flint.)



FIG. 60.—Section of tumor, showing several giant cells in the midst of an endotheliomatous type of growth. ($\times 250$.) (Stewart and Flint.)

Pathologically, the chief interest is in regard to the giant cells and the cholesterol crystals. Apparently, the cholesterol has nothing to do with the giant cell formation.

In American literature, Beekman¹ reports 3 cases of giant-cell tumors

¹ *Annals of Surgery*, 1915, lxii, 738.

of the tendon sheaths from the pathological laboratory of the New York Hospital, and gives photomicrographs. He then summarizes the literature. It is very gratifying to me to find that this author adopts the term giant-cell tumor and drops the word sarcoma. In the articles of Stewart and Flint and of Beekman, and in the references which I have given in *PROGRESSIVE MEDICINE*, one will find practically all of the literature on this subject.

These small, more or less encapsulated, giant-cell tumors of the tendon sheaths are not at all different from the fibroma and the fibro-spindle-cell tumor of the tendon sheath, except as to the presence of giant cells. Cholesterin is not always present, and we may find blood pigment in the cases in which we do not find giant cells.



FIG. 61.—Case 2. Section of tumor from peripheral portion of the growth, showing groups of xanthoma or foamy cells. There are no giant cells in this field. ($\times 250$.) (Stewart and Flint.)

The tendon-sheath tumor which I¹ reported in 1903 is a large edition of the giant-cell tumor described by Stewart and Beekman. Here the tumor was diffuse, involving the tendon sheaths of the ankle. Since this case was reported, Reid,² who has specially studied this group, is of the opinion that it is a xanthoma.

When this tumor was removed in 1897, it was diagnosed sarcoma in the Pathological Laboratory. When I restudied these cases in 1901, I placed it with hemangioma of the so-called elephantiasis or fibroma

¹ *PROGRESSIVE MEDICINE*, December, 1903, p. 154, Pathol. No. 1620, Figs. 16 and 17.

² Landois and Reid, *Beitr. z. klin. Chir.*, 1914, xcv, 56.

type. These tumors show a mottled, white and dark tissue; they are filled with blood pigment, and one can see evidence of bloodvessels, although in this late stage they may all be plugged with endothelial cells. I have seen other cases similar to Pathol. No. 1620. I am impressed with the fact that when this tumor originates on the tendon sheaths higher up, it always forms a larger growth.

The case reported by Fritsch is different from all others in the diffuseness of the growth, extending from the tendon sheaths of the palm of the hand beneath the annular ligament along the tendon sheaths of the arm. My personal experience with these tendon-sheath tumors forces me to the conclusion that they are of traumatic origin and represent granulation tissue—the reaction to a trauma—in which, however, there is not the usual return to scar tissue, but the development of a newgrowth in which vascularity at first predominates; then, due to interference with circulation, there is increase of connective tissue between vessels, plugging of the vessels with endothelial cells, hemorrhage with resultant pigment and giant cells, and in some cases with the deposit of cholesterol crystals. We could imagine that the size of such a tumor, and even its shape, might be influenced by its position, and we can also see how the different histological types from a pure fibroma to a giant-cell tumor and xanthoma might be produced, all from the same original granulation tissue. Apparently, when the granulation-tissue tumor has reached the stage of a fibroma, or a giant-cell tumor, or a xanthoma, the tendency to sarcoma is very much less, or even lost. From my studies of sarcoma of the soft parts after trauma one could rarely gather from the history or the pathological examination, any evidence of a preëxisting tumor of this kind.

Practically, it is very important to bear in mind the benign type of giant-cell tumor or xanthoma, because, when it occurs in regions higher than the fingers or toes, it must be differentiated from sarcoma, or unnecessary amputations will be performed. In the two cases which I reported in 1903, amputations would have been performed if the patients had consented. Both tumors were incompletely removed, but there is no recurrence now in either case about seventeen and twenty-one years since operation. I would advise every surgeon and pathologist to learn by heart the lesson of the tumor Pathol. Nos. 1620 and 3890.¹

THE BONES.

Exostoses. MULTIPLE LESIONS. Ashhurst,² of Philadelphia, is of the opinion that this congenital bone lesion is more overlooked than rare, as he has seen 11 cases in ten years. He agrees with Lenormant that the

¹ PROGRESSIVE MEDICINE, December, 1903, p. 154.

² Annals of Surgery, 1916, lxiii, 167.

exostosis is a secondary change and that the primary is really a hereditary deforming chondrodysplasia. The metaphyses of the bone are chiefly involved. The disease rests upon irregularly distributed areas of cartilage with which there may be associated secondary cysts; later, the growth and ossification of cartilage produce the cartilaginous exostoses. Ashhurst gives excellent illustrations and *x*-rays, with references to five monographic articles on the subject.



FIG. 62.—Traumatic hyperostosis of the humerus, four months after a fall on elbow. (Ashhurst.)

SINGLE LESIONS. In contrast to the multiple congenital type, Ashhurst reports two examples of the single exostosis—one associated with trauma and one with arthritis. Fig. 62 is the *x*-ray picture of a periosteal growth from the lower end of the humerus. There was a history of injury four months before. The *x*-ray at that time showed no fracture; there may have been dislocation. The discomfort after the injury never disappeared. At the operation, the bony growth rested on the shaft of the humerus. It was covered by periosteum, practically excluding ossifying myositis. Gross and microscopically, it consisted of cancellous bone. It is interesting to note that there was temporary recurrence within a month, but nine months later the recurrent periosteal bone had disappeared.

This is a very important observation. After traumatism, with or without dislocation and rarely associated with fracture, we may observe an ossifying periostitis or an ossifying myositis. In many cases much of the bone disappears if the condition is left alone; if possible, therefore, it is the better plan to wait and observe what happens naturally. The great probabilities in Ashhurst's case are that the periosteal bone growth might have disappeared spontaneously without operation.

In his second case, the osteophytes or exostoses were associated with a chronic arthritis of the shoulder in a male patient, aged sixty-two years, who gave a history of injury fifteen years previously. Apparently, there was no fracture or dislocation, but the patient has never been free from

pain since. About eight months before the admission to the clinic, while working at making brooms, he felt a certain crack with immediate loss of function; pain on any motion has prevented work since. At the examination there was no restriction of passive motion, but distinct crackling on external rotation. The *x*-ray showed only some thickened bone about the acromio-clavicular joint. A diagnosis of chronic bursitis was made. At the exploration, no bursa was found; on opening the thin capsule of the shoulder-joint, the head of the humerus was eroded and flattened, and there were two osteophytes at the margin of the articular cartilage. They were about 6 to 7 mm. in height. These pieces of bone were removed, with complete relief of pain, restoration of function, and the result has remained good now two years.

In this case the bone formation undoubtedly was of long duration, probably due to the original injury fifteen years ago, and responsible for the patient's painful shoulder since. The gross findings on opening the joint, described by Ashhurst, picture what we might call chronic arthritis deformans. When single joints are involved, the etiological factor is usually local. In the majority of cases there is first a trauma which produces some joint defect, either by the initial injury, or the scar formation of the healing of the initial wound. Cases of this kind are frequently associated with osteophytes, with loose bone and cartilage bodies, with chronic hydrops; with varying degrees of destruction of the articular cartilage; with flattening and other deforming changes in the head of the bone, and now and then the bone in the joint may show changes such as eburnation or porosis.

Bone Cysts. BONE CYSTS AND OSTITIS FIBROSA. It is of interest to note that this subject was introduced in my first contribution to *PROGRESSIVE MEDICINE*, December, 1899, p. 236, and since then I have kept up pretty well with the literature. My own monograph appeared in 1910. Müller¹ had previously, however, gone over the literature in 1906. Silver² also gave us a very excellent summary in 1912. Then in 1914, Landon³ contributes an excellent summary up to date and reports a number of interesting cases. There is now, therefore, in American literature an easily accessible number of very good contributions on bone cysts and ostitis fibrosa cystica, and we should not forget that Carl Beck,⁴ of New York, was one of the first, if not the first, to report a case in American literature and then Corson,⁵ of Savannah, reported his case in 1902. The articles of Blake, Codman, Kammerer, and Müller appeared later.

It has always been gratifying to my sense of preparedness that I was able to anticipate this disease from the studies of the literature, which I

¹ University of Pennsylvania Medical Bulletin, September, 1906, p. 173.

² American Journal of Orthopedic Surgery, 1911-1912, ix, 563.

³ Annals of Surgery, 1914, lx, 570.

⁴ American Journal of Medical Sciences, 1901, cxxi, 666.

⁵ Annals of Surgery, 1902, xxv, 505.

have first reported here in 1899, and from those studies was able to recognize my first case in 1903.

From France we have the monograph of Bérard and Alamartine.¹ From the two excellent reviews of this article which I have read, I infer that they cover the old ground of history beginning with Virchow, and then discuss the various theories as to etiology, differential diagnosis, and report cases. But in their monograph there is nothing essentially new, although their personal opinion favors insufficient thyroid secretion as a etiologic factor. Then there are two German articles which go over the subject in about the same way by Kolaczek² and Bolognesi.³

BONE GRAFT. Frank S. Mathews⁴ mentions a bone cyst of the shaft of the humerus in a boy of thirteen. At operation the bone shell was "as thin as paper." Instead of resecting in continuity, Mathews simply transplanted into the cavity a piece of bone chiselled from the shaft of the tibia. Firm union resulted. In this case the boy had had pain in the arm for some months before he sustained the fracture.

I am inclined to think, when we begin to take x-rays for pain in the bones of children, the number of our cases of bone cysts will increase. I am sorry that Mathews does not report on the microscopic appearance of a blood clot which he found in this cyst. He states that there was solid tissue in the lower portion of the cyst, which was reported from the laboratory to be *ostitis fibrosa*. I⁵ have previously reported a similar case in which a piece of the tibia was transplanted into the bone cyst of the humerus.

OSTITIS FIBROSA WITHOUT CYSTS. Kammerer,⁶ in discussing Mathews's bone cyst of the humerus, refers to the case reported by him⁷ in 1904. Here the marrow cavity of the femur was entirely filled with solid, white tissue, and there were no cysts. The patient came under Kammerer's observation with a pathological fracture which had occurred two years before, and which had united and recently refractured. He states that this patient is apparently well now, many years since the first observation.

Ostitis fibrosa of this type in a single bone is unusual. When I⁸ made my report in 1910 I could find but 7 cases. Kammerer's case (Pathol. No. 5699) is pictured in Figs. 63 and 64. In 6 cases the condition was very similar to that in Kammerer's observation, except there was one or more small cysts (Fig. 65) in Halsted's case (Pathol. No. 5358). This is

¹ *Rev. de Chir.*, August, 1914–November, 1915; review in *Journal of the American Medical Association*, 1916, lxvi, 538; *Surgery, Gynecology and Obstetrics*, 1916, xxii, abstr. p. 388.

² *Beitr. z. klin. Chir.*, 1914, xc, 588.

³ *Deutsche Ztschr. f. Chir.*, 1914, cxxxi, 382.

⁴ *Annals of Surgery*, 1915, lxii, 625.

⁵ *PROGRESSIVE MEDICINE*, December, 1912, p. 310, Fig. 56.

⁶ *Annals of Surgery*, 1915, lxii, 625.

⁷ *Ibid.*, 1904, xxxix, 105.

⁸ *Ibid.*, 1910, lxii, 148.

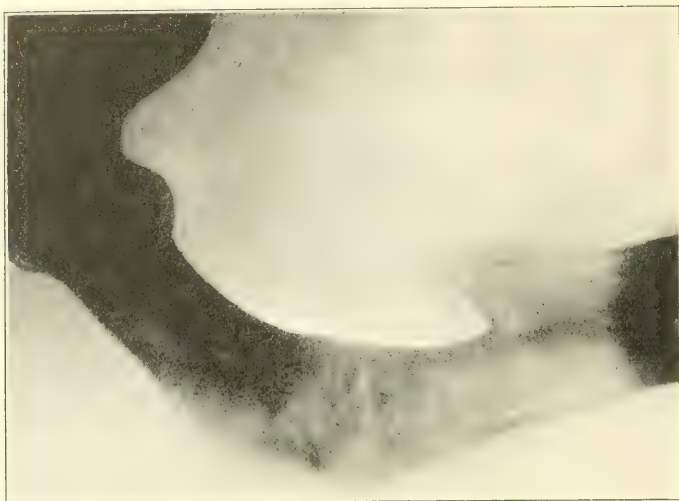


FIG. 63.—Pathological No. 5699. Ostitis fibrosa of femur, no cysts. White male under twenty years of age; fracture some years ago; for five months since heavy lifting pain, limp, angular deformity. The *x*-ray shows a shadow similar to Fig. 5, and a pathologic fracture. The solid fibrous tissue filling the marrow cavity of the femur was removed with the curette by Dr. Kammerer of New York, in November, 1903. 1910—six and one-half years well. (See Fig. 64.)

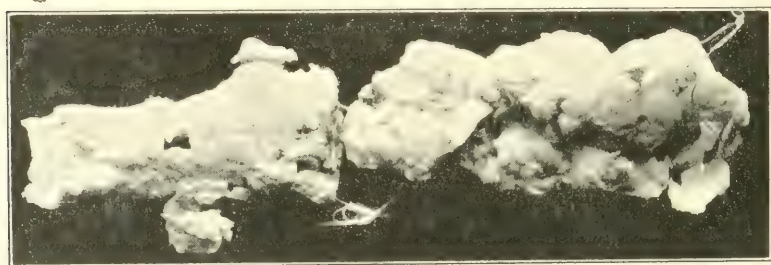


FIG. 64.—Pathological No. 5699. Specimen removed by Dr. Kammerer from case illustrated in Fig. 63. This is the gross appearance of ostitis fibrosa. Compare with Fig. 65.

such an unusual picture, and since I know of recent cases in which this marrow lesion has been looked upon as sarcoma,¹ I think it important to reproduce some of these illustrations again. The microscopic appearance is shown in Figs. 66, 67, 68, and 69.

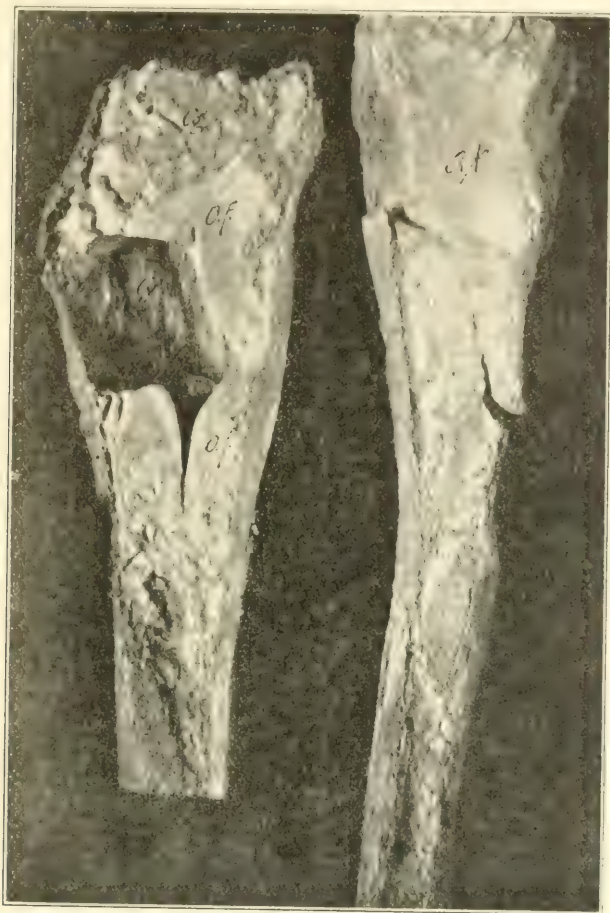


FIG. 65.—Pathological No. 5358. *Cg*, cartilage near epiphysis; *O. f.*, osteitis fibrosa; *Cy*, cyst. The bone shell is everywhere preserved. April, 1910, six years well. Complete restoration of femur from periosteum.

TRANSPLANTATION OF FAT. I refer to the case reported by McArthur² chiefly to advise against the routine treatment of bone cysts by filling the bone cavity with anything. In McArthur's case the cyst was in the lower end of the fibula. Its fibrocystic contents were shelled out in a solid lump; the cavity was filled with a mass of fat from the thigh.

¹ Hitzrot, *Annals of Surgery*, 1915, lxi, 742.

² *Surgery, Gynecology and Obstetrics*, 1915, xxi, 533.

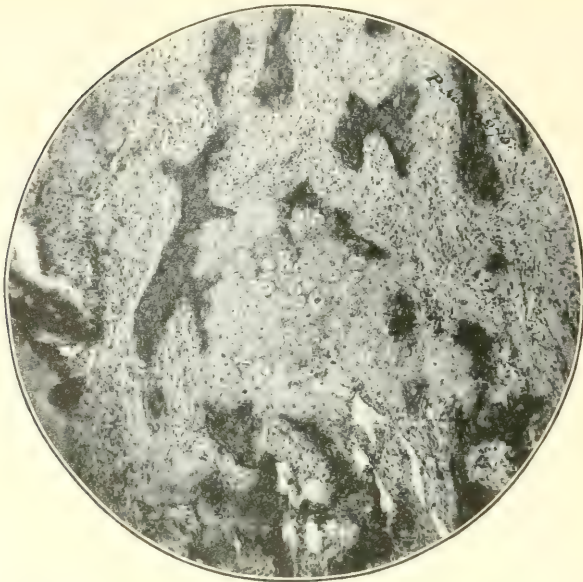


FIG. 66.—Pathological No. 10275. Photomicrograph by Schapiro, showing islands of cartilage in the bone shell in which the bone lamellæ are separated by ostitis fibrosa. Patient of Dr. Leary of Boston. White girl, aged five and a half years; contusion of humerus two years without symptoms; recent injury (three days), fracture, x-ray very much like Fig. 1. Cyst in humerus extending to epiphysis. Operation January, 1910, curetting, the cyst contained no connective-tissue lining.

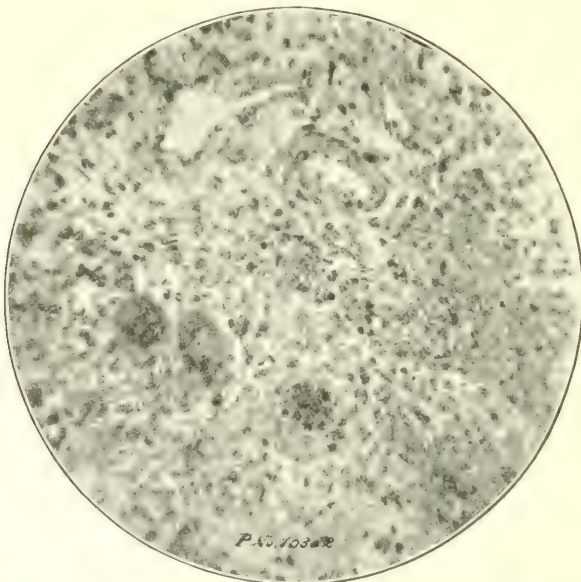


FIG. 67.—Pathological No. 10352. Giant cells in a hemorrhagic area of ostitis fibrosa. Bone cyst of the humerus in which there was a definite connective-tissue lining. (Eisendrath's second case.)

McArthur writes: "One should not hesitate in case of a bone cyst to fill in the cavity with a Mosetig-Moorhof plug, with Beck's paste, or with any other material that will obliterate the cavity. It is better than the blood clot that has been so frequently recommended."

From a very large experience with bone cysts, which have been published in the December numbers of *PROGRESSIVE MEDICINE* and reported in a monograph in 1910 (loc. cit.), I am convinced that in the majority of cases simple curetting of the cavity is sufficient. In some of the larger cysts, the shell of bone may be crushed in. I personally have had but one recurrence, and in this case at the second operation I transplanted a

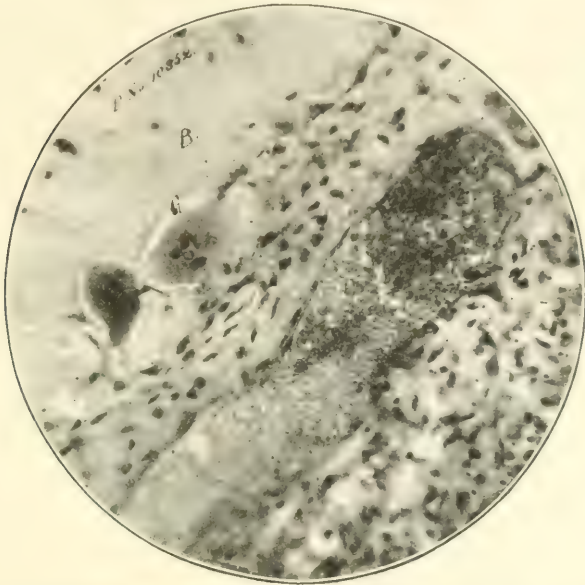


FIG. 68.—Pathological No. 10352. Photomicrograph (high power) of the bone shell (*B*), the giant-cell osteoclasts (*G*) and a very vascular area of the connective-tissue lining. (Eisendrath's second case, see Fig. 67.)

piece of bone into the cavity in the humerus. Fig. 70 pictures a cyst I operated on in 1903. In this instance there was no connective-tissue lining. All that was done was to let out the fluid and close the wound. Fig. 71 pictures the same humerus seven years later. It may be observed that the continuity of the shaft of the bone is absolutely restored.

The evidence, therefore, up to the present time is against filling these cavities, after bone operations, with any foreign material, or transplanted tissue. In recurrent cases it might be well to try transplantation. Of course, it is simpler to fill the bone cavity with a piece of fat than with a piece of bone, but, personally, and from the literature, the evidence in

favor of Makkas's¹ method is not as yet sufficient to justify its employment for bone cavities. In McArthur's observation, but four weeks have elapsed since operation.

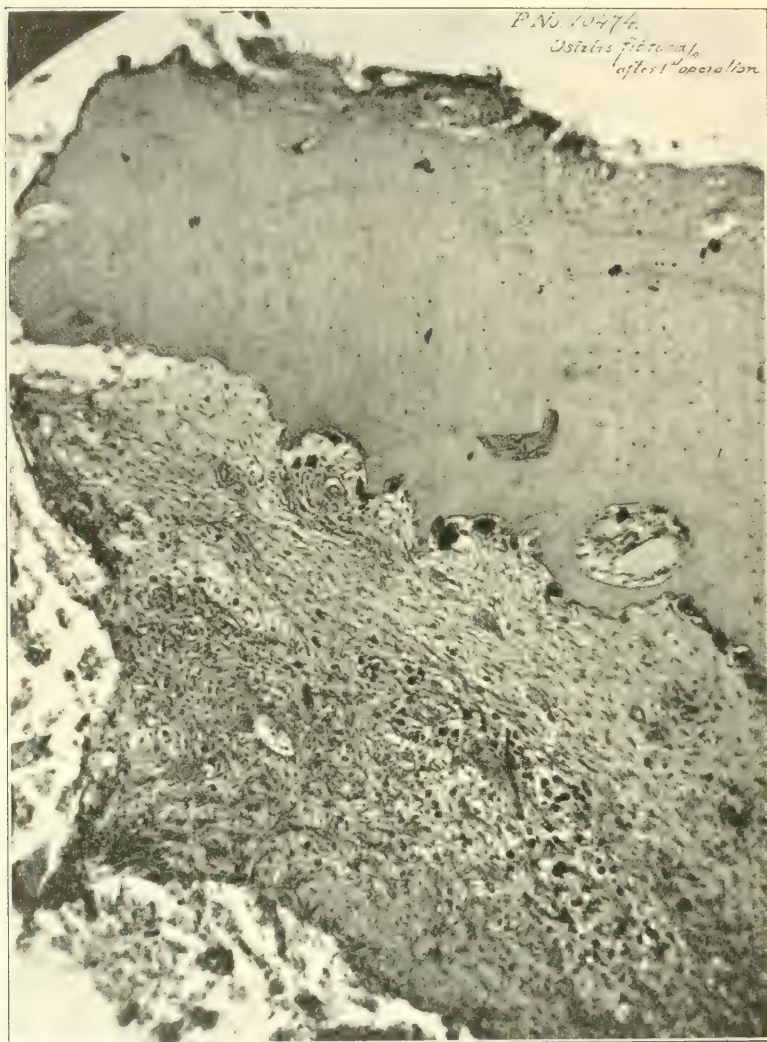


FIG. 69.—Pathological No. 10474. Photomicrograph (low power) from section of bone shell and connective-tissue lining (Sowers's case). Note the giant-cell osteoclasts producing bone absorption.

Skinner² in reporting 5 cases rather favors filling of the cavity with a Mosetig-Moorhof paste.

¹ PROGRESSIVE MEDICINE, December, 1914, p. 294.

² Surgery, Gynecology and Obstetrics, 1915, xx, 570.

MULTIPLE BONE CYSTS. Kanavel¹ made a brief report before the Chicago Surgical Society in which he considered chiefly the question of operation for multiple bone cysts. The patient was an adult and when he came under observation he gave the history of a bone cyst in the femur eight and one-half years before, and that this lesion had kept him confined to a hospital for six years. There was apparently a free interval of about eighteen months, when he returned with pain in the legs. Kanavel could get but little help from the literature, but he reasoned

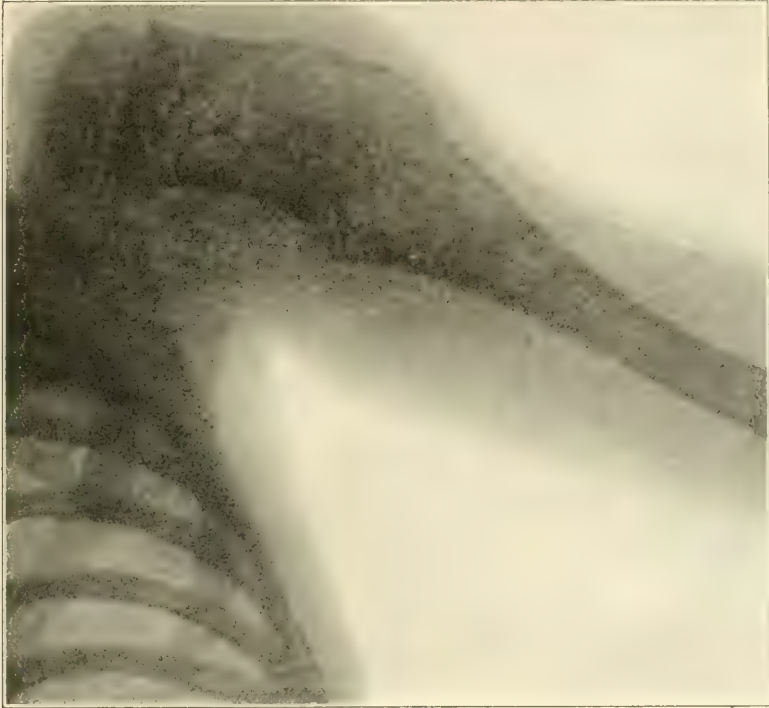


FIG. 70.—Pathological No. 4993. Bone cyst of humerus; no connective-tissue lining. White female, aged seven years; history of fracture one year ago with healing; recent fracture four days, pain and loss of function. 1903 curetting (Bloodgood). 1910 well. (See Fig. 71, X, fracture.) Photograph of patient shows result three months after operation.

that if curetting helped one cyst, it might relieve many cysts. In his case the curetting of two cysts gave immediate relief from pain. The man apparently had other and older cysts, some of which could be palpated on account of the bone expansion, others could be seen in the *x*-rays. In the two cysts operated upon, there was bone tissue filling the cavity. Kanavel states that his patient was well at the time of the

¹ Surgery, Gynecology and Obstetrics, 1915, xx, 745.

report one year and one-half later. The cysts which were not painful were not operated on. I note with great interest Kanavel's statement that in one of the cysts which he curetted there was sufficient bleeding to make packing necessary, while the other was closed. I shall call attention to the danger of bleeding in large cysts on another page. Straus also presented a case of multiple bone cysts at this meeting. Straus apparently examined also the tissue from Kanavel's case. He speaks of seeing cartilage formation, giant-cell areas, fibrous areas with few or no giant cells; as a rule, where there was much hemorrhage there were many giant cells.



FIG. 71.—Pathological No. 4993. X-ray seven years after operation in case illustrated in Fig. 70.

SUBPERIOSTEAL RESECTION. Skinner,¹ in discussing the treatment of bone cysts, quotes Murphy, of Chicago. The latter favors the transplantation of a piece of bone into the cyst when there is a fairly good bone shell, but in cases of considerable expansion and deformity there should be a subperiosteal resection with transplantation. Murphy and Goldman have had some brilliant results.

In spite of these impressive results and in spite of the advice of Albee, of New York, I would urge my readers not to attempt resection for a benign bone cyst as a primary operation. I have never had to resort to it. Those who have performed it have done so as a primary measure with no evidence, as far as I can gather, to justify the procedure. It

¹ Surgery, Gynecology and Obstetrics, 1915, xx, 570.

makes a longer convalescence, and the risk of bad function is greater. I have just had some correspondence with Dr. Hoke, of Atlanta, Georgia. He sent me *x*-rays of 2 cases, both apparently marrow tumors in the upper end of the tibia. In both cases the cavities were smaller and the bone shell thicker than cases of giant-cell sarcoma and bone cysts cured by curetting. Hoke resected his first case and transplanted bone, but at the present time—over one year—there is not perfect function. He asked me what I would advise in the second case. My answer is given above. Yet Albee, of New York, from the same evidence, advised resection and bone transplantation.

SARCOMA. Fully developed malignant disease and the common diseases found at autopsy have a pretty distinct histological picture. But since surgery stepped in, tissue has been removed in the operating room with which pathologists had little or no familiarity, either from the literature or from autopsy. This is true of *ostitis fibrosa*. Virchow, many years ago, observed a cyst surrounded by a zone of cartilage in the upper end of the humerus. When I collected the cases in 1910, there were but 3 additional cases similar to Virchow's first, while I found 85 cases not associated with cartilage; 69 were true examples of *ostitis fibrosa*, 5 were pure myxomas, 4 were cysts in giant-cell sarcoma; in 4 cases the bone lesion was *ostitis deformans*; there were 2 examples of the rare ossifying subperiosteal hematoma, and 1 example of a still rarer lesion—a callus cyst. Since then the number of cysts in *ostitis fibrosa* has increased tremendously. The point, however, that I wish to emphasize is that we must be very careful in our attitude toward the microscopic diagnosis from frozen sections of unusual tissue. For example, Hitzrot¹ observed a case of fracture of the left humerus in the Cornell Division of the New York Hospital in May, 1914. When the routine *x*-ray of the fracture was taken, he found a bone cyst with a pathological fracture. Within nine days after the trauma, he cut down upon the fracture in the bone cyst and was very much impressed with a viscid, gummy material extending from the medullary cavity into the surrounding muscle; the adjacent muscle tissue seemed infiltrated by a mass of more or less homogeneous cartilage-like material. Frozen sections were made, and the report was myxochondrosarcoma. The surgeon apparently was in a dilemma. He knew that if that was a sarcoma infiltrating all the muscles an amputation was indicated, but he writes: "In view of the doubtful pathology of these lesions in general and in spite of the pathological report, it seemed wisest to first try conservative measures before resorting to an amputation." However, he did not have the courage of his convictions: while he did not amputate, he did perform a wide resection on muscle and bone, and then filled the defect with a transplant from the tibia. In twelve weeks there was complete use of the arm.

¹ *Annals of Surgery*, 1915, lxi, 742.

I am confident that cases of this kind are occurring every day, because it seems impossible to keep up with what the *x*-ray finds and to learn the new histological picture of the early stages of diseases with which we were perfectly familiar only at a later stage and with a different microscopic appearance.

I think, in this case, we may say with Hitzrot that before the days of the *x*-rays this patient would have been treated for an ordinary fracture, the bone cyst would have healed, and no one would have been aware of its existence. If he had come under observation at the beginning of the *x*-rays, the picture of the marrow tumor with its bone shell would have excited the curiosity of both the röntgenologist and the surgeon. The probable diagnosis of a sarcoma would have been made and amputation might have been suggested. This is the story in all the early cases. But, in 1914, the condition was diagnosed from the *x*-ray plate and the surgeon operated, but then he exposed an unusual gross picture of the surrounding muscles near the fracture. I have not seen the microscopic sections in this case, but I have seen a similar picture, when the bone cyst was exposed shortly after trauma or fracture. The marrow cavity is filled with organizing blood clot, the surrounding muscles show myositis with different forms of degeneration. Here we have a granulation tissue not unlike sarcoma, edema suggesting myxoma and isolated plasma cells that might be mistaken for cartilage. Of course, the result in Hitzrot's case will establish the correct diagnosis. I have never observed a sarcoma of bone infiltrating muscle, as in this case, cured even by the highest amputation, and, judging from his description, I have never seen a sarcoma associated with a cyst of this kind. But, whether it is sarcoma, or not, it is a good demonstration of how our diagnostic dilemmas are increasing and how much more we must familiarize ourselves with all the possible data not only from cases in our own experience and reported in the literature, but there must be an exchange among surgeons and pathologists of rare and unusual material and cases. The decision in surgery as to what to do must be influenced by many factors, and in many instances the frozen section is the least helpful; in fact, in the hands of an inexperienced pathologist, it may prove more dangerous to the patient than the action of an inexperienced surgeon.

BONE CYST IN CONGENITAL FRACTURE. Stierling¹ reports the first case of a bone cyst in a congenital fracture. The child was five weeks of age when seen; the deformity of the fracture was present at birth, and the mother then remembered a contusion of the abdomen before labor. The *x*-ray (Fig. 72) shows fracture, with bending of, and the light shadows in, both bones. From the gross description there was no well-defined cyst, but bone had been replaced by the *ostitis fibrosa* tissue.

¹ *Deutsche Ztschr. f. Chir.*, 1914, cxxx, 85.

The microscopic appearance is most carefully described, and it seems to answer the requirements of an exact diagnosis.

From my experience there were, perhaps, more small cysts in this case than usual. According to Stierling, the diagnosis of *ostitis fibrosa*, according to von Recklinghausen, should only be made when the following histological pictures are found:

Fibrillar connective tissue containing a few spindle and star-like cells, and with very few vessels; osteoclasts or giant cells in heaps or nests; old bone lamellæ still containing calcium and new osteoid tissue without calcium.



FIG. 72.—Bone cyst in congenital fracture. (Stierling.)

It is important for other pathologists to read what Stierling considers was von Recklinghausen's conception of *ostitis fibrosa*. In my experience, the most important of these three requirements is the first. When we make a section of the bone shell, of course, we always find the old bone lamellæ, but we do not always find new osteoid tissue; this is found as in Stierling's case, where there was a recent fracture. The giant cells vary, and we find them not only between the fibrous tissue and the bone shell, but in blood clot.

One interested in this histological picture may refer to my illustrations (Figs. 66, 67, 68, and 69).

It is interesting to note that this patient was observed three years later: There was little or no shortening, no deformity, but in the region of the old fracture still some light shadow in the bones.

BONE CYSTS OF THE UPPER END OF THE FEMUR. The case reported by Domingo¹ is of interest on account of its location and because the tumor was multicystic. At the examination, the swelling was beneath

¹ *Surgery, Gynecology and Obstetrics*, 1913, xvii, abstr. p. 409.

Poupart's ligament, and the great trochanter, on palpation, was enlarged. The *x*-ray showed a tumor the size of an orange surrounding the upper end of the head of the femur to the trochanter. At operation, the tumor was multicystic, contained bloody fluid, and was filled with soft spongy material; microscopically—enchondroma. If this microscopic examination is correct, we are not dealing with a true bone cyst, but a cystic enchondroma. Trauma was the etiological factor in this case, and the symptoms had been present more than four years; swelling had been observed but one year. If we use the term bone cyst in its broader sense, as I employed it in my original article, this is a bone cyst, but not of the type associated with *ostitis fibrosa*. From the meager pathological report, we would not know just where to place it, but it might be another example of a callus cyst.



FIG. 73.—*Ostitis fibrosa cystica* of second metacarpal bone. (Landon.)

BONE CYST OF THE METACARPUS. The case reported by Landon¹ is, in my experience, unique on account of the involvement of the entire metacarpus. In fact, the *x*-ray shadow (Fig. 73) rather suggests osteomyelitis. It is quite possible that this peculiar picture and extent of the disease may have been influenced by treatment. The male patient, aged twenty years, had observed a swelling in the region of this bone at the age of five. There have been two operations, the last three years ago. The wounds had healed. The recurrence of symptoms followed an

¹ *Annals of Surgery*, 1914, lx, 570.

injury two weeks before the patient came under observation. As the patient was illiterate, no other details in his history could be obtained. The bone could be felt to be distinctly enlarged. At the operation, the periosteum seemed normal; the enlarged bone looked worm-eaten and bled easily. There were numerous cavities with thin, fragile walls, with gelatinous contents. There was evidence of calcification and new fibrous tissue beneath the periosteum; the articular cartilage was normal. We have, therefore, a multicystic bone lesion. The microscopic study revealed *ostitis fibrosa cystica*.

I have observed one case somewhat similar to this.

Ostitis Deformans. Osteomalacia, *ostitis deformans* and *ostitis fibrosa* may affect many of the bones of the skeleton. Cysts may occur, most frequently in *ostitis fibrosa*, and there may also be currant-jelly tumors, histologically identical with the giant-cell tumor. In the literature examples are reported of osteomalacia confined to a single bone. In the older literature on coxa vara, bending, in non-traumatic cases, was attributed to localized osteomalacia. There were even cases reported with histological examination. I have never observed a case personally. The localization, however, of osteomalacia and *ostitis deformans* in a single bone is a thoroughly established fact. There are some authorities who believe that *ostitis deformans* represents the healing stage of *ostitis fibrosa*. In *ostitis deformans* there is always bending, and it seems difficult to understand how such bending could take place without a bone lesion associated with softening of the bone. This could be easily associated with *ostitis fibrosa* or osteomalacia. Then the ossification of the thickened and bent bone would give the picture of *ostitis deformans*. The cases of *ostitis deformans* localized in one bone which I have seen had been present years, and this is true of the cases reported in the literature. Landon¹ illustrates an x-ray (Fig. 74) with the following legend: *Ostitis deformans* of the femur; note great thickening and overgrowth of bone with rarefaction and eburnation occurring simultaneously. This picture may be considered further evidence of the relationship between these two bone lesions. Bockenheimer holds this view also.

It is rather interesting that, in the review by Jefferson,² he states that Ellis, in 1910, collected about 158 cases, while in the report of 1915 from Da Costa, Funk, Bergeim and Hawk,³ they find only 158 cases. My familiarity with the literature could easily explain this apparent discrepancy. Both investigators undoubtedly have cases from different sources overlooked by each. Then, again, references are confusing. These two reviews add nothing particularly new to the older literature. Both find that the Wassermann reaction is usually negative. Jefferson looks upon Paget's disease as due to a disturbance of internal secretion,

¹ *Annals of Surgery*, 1914, lx, 570.

² *Loc. cit.*

³ *Loc. cit.*

especially the thyreo-parathyroid, and he would expect benefit from the extract of these glands. Da Costa and his collaborators are rather inclined to share this view, especially as to the relation between the parathyroid and calcium metabolism.

The time is coming when we will see, and be able to recognize, these cases earlier. Then there will be a better opportunity to get at the etiological factors and probably a better chance to find some therapeutic agent for good.

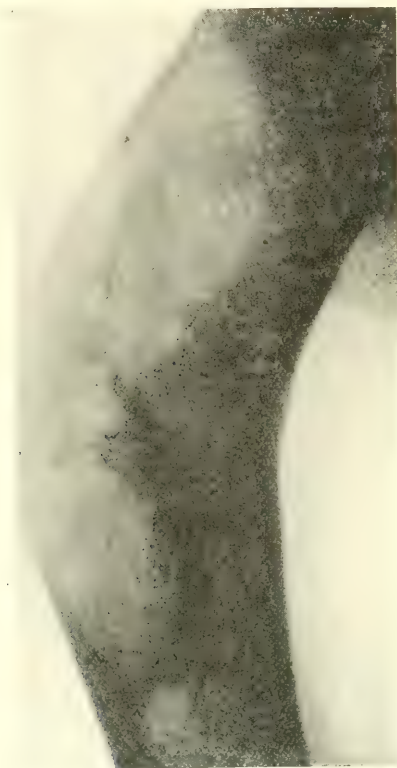


FIG. 74.—Radiogram in case of *ostitis deformans* of femur. Note great thickening and overgrowth of bone with rarefaction and eburnation occurring simultaneously. Male. (Landon.)

The case reported by Moschcowitz¹ is interesting because the symptom of onset was enlargement first of the right parietal bone and then of the superior maxillary. In addition, there is a complete report on x-ray studies of all the bones. The röntgenologist Hirsch apparently is of the opinion that there is a close relationship between *ostitis deformans* and *ostitis fibrosa*. There are no illustrations reproduced with this report.

¹ *Annals of Surgery*, 1914, lx, 375.

OSTITIS DEFORMANS AND SARCOMA. Da Costa, Funk and Bergeim,¹ in reporting 3 cases of Paget's disease among 38,000 patients admitted to the Jefferson Hospital in Philadelphia, tabulate in all 158 cases. Among these, 14 patients developed sarcoma of bone, and, of the 8 patients traced to the end, 5 died of sarcoma. A proportion of 5 bone sarcomas among 158 individuals is apparently a very large per cent., so large that it is a question whether Paget's disease should not be looked upon as a form of chronic osteitis predisposing to sarcoma. Up to the present time the only etiological factor which stands out prominently in sarcoma of bone is a trauma of the contusion type without external wound and rarely associated with fracture or dislocation. We have no observations associating sarcoma with either tubercular or pyogenic osteomyelitis, nor with syphilitic periostitis, and here for the first time we have evidence associating sarcoma with Paget's disease.

I have within the past two years observed a periosteal myxosarcoma apparently secondary to an old case of Paget's disease localized in the left tibia. This patient died of metastatic sarcoma after a high amputation.

In a second report on Paget's disease by Jefferson,² there is no note in the review about any cases of sarcoma, and I have not the opportunity now to get the original.

I have just noticed that Da Costa and Jefferson favor the relation between osteitis deformans and some deficiency in the thyroid or parathyroid secretion, while Moschcowitz states that favorable results have been reported from pituitary extract.

Osteomalacia. Landon³ is of the opinion that Fig. 75 represents osteomalacia with cyst formation. These pictures were taken from a child, aged one year, who came into the clinic because of a fracture of the femur.

Molineus⁴ reports 3 cases of a general disease of the skeleton in which there were multiple giant-cell tumors. He was rather inclined to consider his cases as osteomalacia, or osteitis fibrosa atrophica, in contrast to the osteitis fibrosa hypertrophica of von Recklinghausen. He also states that in his cases there was a definite hyperplasia of the parathyroids.

The literature to which he refers is that with which we are familiar, and we must remember that Rehn, in reporting his example of multiple giant-cell tumor, looked upon the disease as osteitis deformans, while Haussling and Martland⁵ are convinced that their example of multiple

¹ Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 60.

² British Journal of Surgery, 1915, iii, 219; review in Surgery, Gynecology and Obstetrics, 1916, xxii, abstr. p. 264.

³ Loc. cit.

⁴ Archiv. f. klin. Chir., 1913, ci, 333; Surgery, Gynecology and Obstetrics, 1913, xvii, abstr. p. 409.

⁵ Annals of Surgery, 1916, lxiii, 454.

giant-cell tumors in bone was associated with von Recklinghausen's *ostitis fibrosa*.

For the past ten years this dilemma between *osteomalacia*, *ostitis fibrosa* and *ostitis deformans* has continued, so that one gets the impression that they may be different stages of a bone lesion having identical etiological factors and, in the very beginning, rather the same clinical manifestations.

The practical point to always bear in mind is this: When the attention is called to a single bone lesion, before treating it, it is well to make an investigation and search for other bone lesions.



FIG. 75.—*Osteomalacia*. Female, aged one year. Shows cystic changes. Note involvement of epiphyses and of left tibia. (Landon.)

Multiple Hemangioma of Bone. Symmers and Vance¹ describe their single observation as multiple primary intravascular hemangio-endothelioma of the osseous system associated with symptoms of multiple myeloma, a lesion hitherto undescribed. Their one microscopic drawing (Fig. 76) pictures a lesion which we may call a hemangioma. In most angiomas there is perithelial and endothelial proliferation. Some of these cases show great increase of the connective tissue—fibrohemangioma; some are deeply stained with blood pigment and may contain cholesterol xanthoma. These various types of hemangioma, some of

¹ American Journal of Medical Sciences, 1916, clii, 28.

which become malignant, have been observed in all tissues, but they are very rare in bone. Howard and Crile¹ give a résumé of endothelioma and perithelioma of bone. They report 4 cases, and collect 19 from the literature.



FIG. 76.—A, capillary distended by red-blood cells and showing a circumferential layer of proliferating endothelium. At one end is a small subsidiary vascular channel lying in the endothelial layer; B, capillary vessel showing the presence of multiple subsidiary vascular channels; C, smaller vessels with their lumina almost completely occluded by proliferating endothelium; D, vessels distended by proliferating endothelial cells with only partial preservation of the lumen, which is occupied by red-blood corpuscles; E, spicules of bone lying in a moderately cellular fibrillar connective tissue. (Drawn with Edinger's apparatus.) (Symmers and Vance.)

The case reported by the authors was that of a male Russian, aged forty-three years: the symptom of onset and chief complaint was pain in the left gluteal region extending up to the tenth dorsal vertebra, and, on examination, there was a painful mass in the left ischio-rectal fossa apparently attached to the tuberosity of the ischium. The *x*-ray showed irregularities in the outlines of the bone in the region of the left ischium. Within two months there was pain and tenderness in other regions, and

¹ *Annals of Surgery*, 1905, xlii, 358; *PROGRESSIVE MEDICINE*, December, 1906, p. 235.

within five months two new tumors; then the *x*-ray revealed other bone lesions. Associated with this there was anemia and emaciation, and, finally, death. There was no autopsy. For the relief of pain before death, the palpable tumors in the ischium, skull and humerus were curetted. The histological picture is shown in the illustration.

In a search of the literature they apparently did not find the contribution of Howard and Crile in 1905, nor any of the older literature reported by them. There is a new case reported by Zetkin—a single tumor in the shaft of the humerus.

From their description and illustration, we have no positive evidence that we are dealing with a sarcoma. This case, like the majority of multiple lesions of the skeleton, is obscure; we do not know the etiological factors, nor why these patients die of anemia and emaciation without metastasis to the viscera.

Giant-cell Tumor. I have often asked myself what became of the bone cysts before the advent of the *x*-rays. The first case of a bone cyst diagnosed and operated upon in the Johns Hopkins Clinic was in 1903. Previous to this, two cases had been admitted: both were huge tumors, were diagnosed sarcoma and refused amputation. This story has been completely told again under bone cysts, and I ventured the opinion that the majority of bone cysts recover spontaneously. I am beginning to feel that there is a relationship between the bone cyst with its *ostitis fibrosa* and the fully developed giant-cell tumor. Perhaps there is a tendency even in the latter for spontaneous healing. It is not impossible that some of our cases of giant-cell tumor which come under our observation with a single lesion had multiple foci in the beginning of the trouble. In Haussling and Martland's¹ second case, the tumor was situated in the lower end of the right tibia. This is not a very common locality. The patient was an Italian barber, aged twenty-eight years. The case is of especial interest because there had been two curettings without a diagnosis. The trouble apparently began after a trauma three and one-half years before he came under the observation of the authors. The first curetting was made a few months after a sprain of the ankle because the swelling did not disappear. Remarkable to relate, there is a free interval of eighteen months, then a recurrence of the pain and swelling, a second curetting followed by freedom from recurrence for seven months.

In a case of my colleague, Dr. Chambers, of Baltimore, which I have reported, there was a free interval of six years between the first and second curetting. In a case of my own observation, there were two curettings and then resection of the lower end of the radius, and now there has been freedom for eight years since I removed the third recurrent tumor.

Haussling and Martland, therefore, in this observation, record more

¹ Loc. cit.

evidence in favor of the benignity of the giant-cell tumor. Three months previous to their operation, and some three years and three months after the original injury, the patient fell, and there was bleeding from the sinus which had remained after the last curetting some seven or eight months before. At the operation, complicated, of course, by two previous curettings, a third curetting of the lower end of the tibia was done. Apparently, between the tumor and the ankle-joint there was but a thin shell of cartilage. This case was curetted a second time in 1911—one year later, and again in five months, and still another time for a recurrence in November, 1911. Then the patient was apparently free to January, 1915—a period of over three years. Then there were symptoms of recurrence for five months, followed by another curetting; motion at ankle-joint still good. The present condition of this patient is shown in Fig. 77 eight years after the onset of the tumor, and yet there is no evidence of metastasis.



FIG. 77.—Showing appearance of leg eight years after onset of tumor. Note open sinus. Recurrence is always on edge of sinus. (Haussling and Martland.)

This second case of Haussling and Martland is also unique in the number of curettings. I should be most interested in studying, microscopically, the tissue from the last two curettings, because I always find giant cells in an old bone cavity, even where the primary operation had been for osteomyelitis and not for giant-cell tumor.

I do not know whether Haussling and Martland have reported all of their observations of giant-cell tumors. If not, they have made a most interesting selection. If these are their only two cases, it is another

demonstration that tumors come under observation with varying pictures. This is so impressive that a student of tumors cannot but conclude that individuals vary in their local and general resistance to tumor growth.

These two authors believe in the benignity of the medullary giant-cell tumor and give reference to the interesting work of George Barrie who has advocated the name *Chronic hemorrhagic osteomyelitis*. Barrie's¹ first article which appeared in 1913 has been reviewed² here.

Barrie also is of the opinion that there is a relationship between osteitis fibrosa and the giant-cell tumor.

Haussling and Martland emphasize the typical gross and microscopic appearance of the giant-cell tumor as so characteristic that any surgeon acquainted with the disease should be able to recognize it at the exploratory incision. I propose to refer to a case a little later in which the curetted tissue sent to my laboratory had all the gross appearance of the giant-cell tumor, but the frozen section revealed not a giant-cell tumor, but a hemorrhagic mixed spindle and round-cell sarcoma. In view of this positive statement, I feel that I must warn my readers that there is a medullary hemorrhagic sarcoma, often cystic, which in the gross may look like the giant-cell tumor, and even in the x-ray in the early cases this cystic hemorrhagic sarcoma (bone aneurism) may produce an expansive swelling with the preservation of a bone shell.³

It is very gratifying to me to read that Haussling and Martland, after considering the evidence, are of the opinion that the giant-cell tumor is relatively benign, that it does not produce metastasis, and that the treatment which should be tried first is conservative—usually curetting. One should also refer to this article for the excellent photomicrographs showing the different pictures in the giant-cell tumor in the case with multiple lesions.

SPONTANEOUS DISAPPEARANCE OF A GIANT-CELL TUMOR. F. Gregory Connell⁴ reports an observation of Oviatt, of Oshkosh, Wisconsin, in which the patient refused operation, and the tumor situated in the upper jaw disappeared. The patient is apparently well eight years later. This patient was a school girl, and there was a bulging tumor of the right upper jaw. The eye protruded, and the bone shell crackled on palpation. An exploratory incision was made into the tumor through the mouth above the alveolar margin, and some granulation tissue removed with the curette for examination. The patient refused further treatment.

I am familiar with this case, as Dr. Oviatt sent me sections and a note about it many years ago. The microscopic picture (Fig. 78) is interpreted by Connell and his pathologist, Bunting, of the University of

¹ *Annals of Surgery*, 1913, lvii, 244.

² *PROGRESSIVE MEDICINE*, December, 1913, p. 291.

³ *Ibid.*, December, 1913, p. 298, Fig. 68.

⁴ *Surgery, Gynecology and Obstetrics*, 1915, xx, 427.

Wisconsin, as a giant-cell sarcoma in which the giant cells are of the foreign-body type. Of course, we have not absolute proof in this case that we are dealing with a giant-cell tumor. In my personal experience, and in the literature, I have been unable to find an example of a giant-cell tumor involving the antrum of the upper jaw. They are even less frequent on the alveolar border of the upper, than of the lower jaw. This tumor has been observed in the body of the lower jaw and in the symphysis. Personally, I have a record of four cases so situated. The other possibility in Connell's case is a dentigerous cyst, a tumor not infrequent in this region. However, I have never observed a giant cell area in dentigerous cysts.

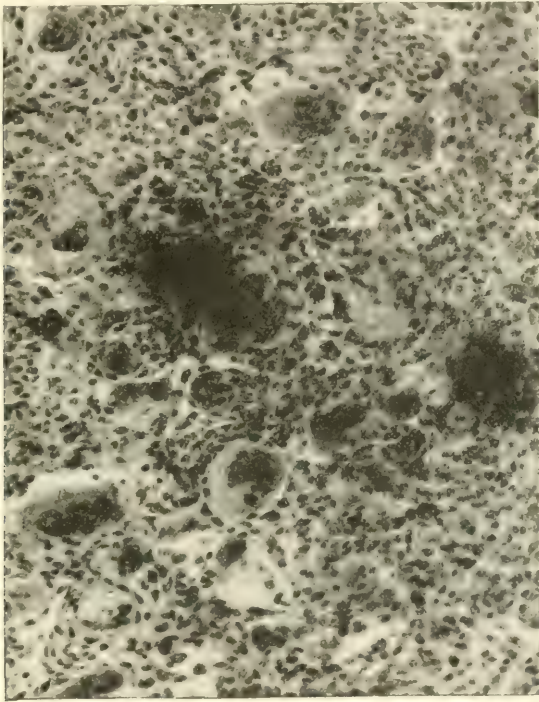


FIG. 78.—Foreign body giant cells. (Connell.)

We know that bone cysts may heal spontaneously. Many are of the opinion that the giant-cell tumor may have some definite relation to the osteitis fibrosa in which the bone cyst develops. So it is quite possible that spontaneous disappearance may occur in the giant-cell tumor.

GIANT-CELL TUMOR. AMPUTATION. Connell,¹ after reporting his case of spontaneous recovery, goes to the other extreme and records an example in which the giant-cell tumor in the head of the tibia had

¹ Loc. cit.

broken through its bone capsule, entered the joint and apparently also the surrounding soft parts.

This local growth, with destruction of the bone capsule and infiltration of the neighboring joint or periperiosteal tissue, is rather the exception in the giant-cell tumor. For this reason, Connell's second operation is worthy of record here. Fig. 79, an *x*-ray, pictures a tumor involving chiefly the inner head of the tibia. The age of the Russian female is not given. The swelling of the upper end of the tibia had been observed seven months. As the tumor became more tense, pain was observed;



FIG. 79.—Case 2 before operation.

for three months she had been unable to walk on account of this pain. There was no fluid in the joint, but motion produced pain. At operation under an Esmarch, the exploratory incision revealed periosteum, but no bone capsule. The tumor was composed of whitish-gray, cheesy material. Now, as a rule, the giant-cell tumor is more hemorrhagic. The cavity, after this material was curetted out, was the size of a golf ball. Its capsule seemed to be composed of joint cartilage, periosteum and normal cancellous bone of the outer head. The cavity, after curetting, was disinfected with carbolic and alcohol. Into the wound was transplanted fat. Closure without drainage. The microscopic picture

(Fig. 80) is interpreted by Oberlin as a typical giant-cell sarcoma. Both tumor and foreign-body giant cells are present.

After operation, the patient still complained bitterly of pain. On the twelfth day, broken down fat discharged from the wound without relief of pain. At the end of four months the wound had filled with granulation tissue, the knee-joint was swollen, and the granulation tissue projected from the wound. The patient was taking morphine for the pain. The x-ray at this time (Fig. 81) shows that the tumor has broken into

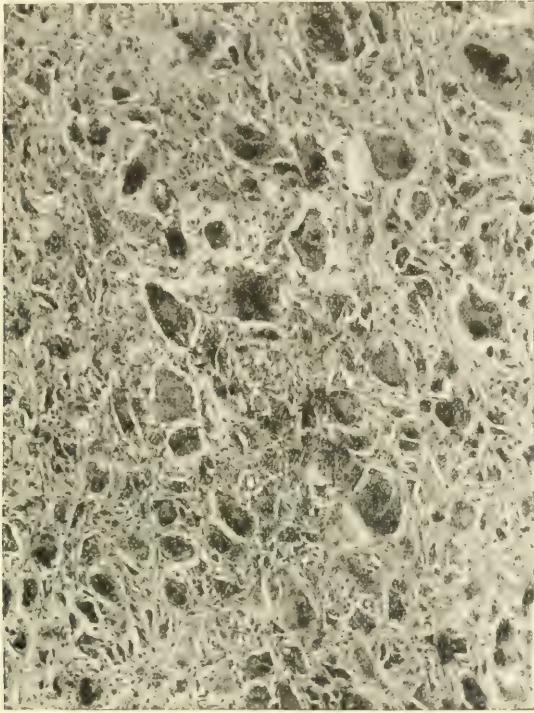


FIG. 80.—Case 2, showing tumor giant cells. Compare with Fig. 3 (photomicrograph by Professor C. H. Bunting of the University of Wisconsin.)

the joint and perhaps invaded the femur. This tumor was first removed locally (Fig. 82), but later, as there was evidence of involvement of the soft parts in the popliteal space, the limb was amputated at the junction of upper and middle third of the femur. The pathological study shows involvement of the lower end of the femur. Amputation relieved the pain.

The unusual clinical feature in Connell's case is the intense pain until the limb was amputated, and second, the small area involved, the lack of expansion of the bone, the absence of a bone shell over the small tumor.



FIG. 81.—Case 2, showing involvement of joint and femur.



FIG. 82.—Case 2, longitudinal section of tumor after amputation. A, granuloma removed at second operation.

However, apparently, microscopically, it is a giant-cell tumor.

Among a number of cases of giant-cell tumor of the lower end of the radius which I have observed, there were two in which the bone shell was pierced and the soft parts infiltrated. In these two cases, there had been repeated traumas and massage. It is many years since the forearms were amputated in these patients, and there has been no recurrence.

In every tumor we see the greatest variation in local growth, both as to time and as to infiltration. The giant-cell tumor is not an exception, although in the majority of cases it tends to expand within its bone shell.

GIANT-CELL TUMOR. RECURRENCE. In studying the *x*-ray of Connell's second case one would consider it as proper for curetting, and Connell after curetting used carbolic and alcohol. Yet, there was almost immediate recurrence, and there was never relief from pain. It would be natural to ask, where the fault lies. We have just mentioned the second case of Haussling and Martland where there was recurrence after repeated curettings of a giant-cell tumor in the lower end of the tibia.

I have recorded a case in which there were recurrences after two curettings and resection for a giant-cell tumor of the lower end of the radius, but this patient remained well after a third operation at which the arm was not amputated.

My colleague, Taylor,¹ of Philadelphia, curetted a giant-cell tumor of the lower end of the femur. He did not employ an Esmarch, the hemorrhage interfered with proper curetting, and there was rapid recurrence. However, the patient is well many years after amputation.

My colleague, Dr. Chambers of Baltimore, has just informed me that a case of his which he curetted six years ago has recently recurred, and he had to resect. The tumor was situated in the upper end of the fibula.

Da Costa curetted a tumor in the inner condyle of the femur; it recurred, but has remained well since local resection.

I² have reported most of these cases in detail. At that time I thought that the failure to use a disinfectant after curetting was responsible for the recurrences, but the cases of Connell and Haussling and Martland, which I have just mentioned, demonstrate that there are other factors. I have studied microscopically the cases which recurred after curetting and compared them with the tumors cured by curetting, and can see no histological difference, nor is there any difference in the gross appearance of these tumors. Therefore, the group of giant-cell tumors which have recurred after curetting should be re-investigated. In Da Costa's, Chambers's, Connell's and Haussling-Martland cases we have tumors which, on the whole, were smaller than those which have remained well after curetting.

¹ PROGRESSIVE MEDICINE, December, 1906, p. 227.

² Annals of Surgery, 1912, lvi, 210.

GIANT-CELL TUMOR OF PELVIS. Guy Blair Denit,¹ before the Philadelphia Academy of Surgery, described a patient from the service of Dr. Ashhurst in the Orthopedic Hospital. The boy was fourteen, and the pain followed a definite trauma. Six weeks before admission, he strained his back; a month later there was a contusion in the right lumbar region. Now the pain confined the boy to bed. He came to the hospital on crutches with the diagnosis of arthritis of the hip. The pain was in the right lower quadrant of the abdomen and in the region of the hip; and in the abdominal quadrant, extending into the lumbar area, there was a palpable mass. Apparently this was explored without first taking an *x*-ray. The gross appearance of the tumor is not described. The report of the laboratory, from the piece removed for diagnosis, was giant-cell sarcoma, and they were of the opinion that it belonged to the myeloid type (after the classification of Stewart).² This patient was given Coley's fluid. In two weeks there was relief from pain, ability to walk, although with a limp. The tumor grew smaller, there was a discharge through the scar, and, when the patient left the hospital eleven months later, the tumor had almost disappeared, and the *x*-ray showed a small tumor near the fourth and fifth lumbar vertebrae. In May, 1915, about one year and five months after the first observation, the boy was apparently well.

Giant-cell tumors in the region of the vertebrae and the pelvis are less frequent than in the long bones. They are very hemorrhagic when explored. They never have the distinct bone capsule of the marrow tumor of the long pipe bone. It is hard to imagine that they can be completely curetted away. The two cases under my observation were incompletely curetted, and are apparently well without any other treatment. Osgood, of Boston, has just related to me a case explored by a surgeon who, on account of the extensive lesion, discontinued the operation and then proposed to the family a very extensive laminectomy. One of the consultants, however, advised delay. The case was carefully studied with the *x*-ray, and the tumor has disappeared.

As I have discussed under recurrences and spontaneous disappearance and amputation, we may repeat here, that the so-called giant-cell tumor, apparently identical in its fresh and microscopic appearance, behaves differently in its local growth, sometimes in the same bone of different individuals, as well as in different bones. Yet, all of these tumors seem to have one thing in common—they do not produce metastasis; at least, the cases under my observation have never metastasized. It should be recorded here, as I have often done before, that some careful observers claim to have seen cases of giant-cell tumors in which after death the autopsy has demonstrated metastases.

¹ *Annals of Surgery*, 1915, lxii, 636.

² *Lancet*, 1914, ii, 1236.

GIANT-CELL TUMOR OF PHALANX. I have seen bone cysts and myomas occurring as marrow tumors of the phalanges. Recently, there was sent to the Surgical Pathological Laboratory, a giant-cell tumor of the end phalanx of the finger. Sievers¹ reports one in the second phalanx of the ring finger. Fig. 83 pictures the *x*-ray, Fig. 84 the specimen removed which is quite like that of a bone cyst, and Fig. 85 the



FIG. 83.—Giant-cell tumor of phalanx. (Sievers.)



FIG. 84.—Giant-cell tumor of phalanx. (Sievers.)

giant-cell tumor and the bone capsule. There was a fracture in this case which healed, so that I am of the opinion that a benign bone cyst cannot be excluded, and I also feel that curetting might have accomplished a cure with much less operative efforts. As I have discussed under bone cysts, we often find giant-cell tissue, especially in the healing stage which is usually induced by a fracture.

¹ Beitr. z. klin. Chir., 1913, lxxxv, 1.

This case is interesting on account of its localization in the phalanx. The man was nineteen years of age and a shoemaker; the symptom of onset was swelling of the left ring finger. There was no pain at first, but within six weeks pain and tenderness forced him to seek the advice of a physician. Within twelve weeks inability to close the hand over a tool brought him to the surgical clinic for relief.



FIG. 85.—Giant-cell tumor of phalanx. (Sievers.)

In my studies¹ of giant-cell tumors up till 1912 I had no record of the giant-cell tumor in a phalanx or metacarpus, nor did I find one in the literature of that time. I see that I overlooked the case reported by

¹ *Annals of Surgery*, 1912, lvi, 210.

Axhausen¹ in which the giant-cell tumor was situated in the basal phalanx of the thumb.

Bone cysts of the type of *ostitis fibrosa* have been observed in the smaller pipe bones, but most frequently when the condition has been multiple. Müller,² in 1906, resected a bone cyst from a metatarsal bone. The cysts situated in the phalanx, which are reported in the literature, have apparently been pure myxomas. In 1910, I collected 5 cases, two of which I was able to examine microscopically. The case mentioned by Sievers, as observed by Boström in 1883, apparently belongs to the type myxoma. It seems rather remarkable that the majority of marrow tumors of the phalanges are myxomatous; of the metatarsal or metacarpal, cysts in *ostitis fibrosa*; and of the lower end of the ulna and radius, giant-cell tumors. However, we need a very much larger collection of cases before we can be certain that this is not accidental.

I have just referred to the bone cyst in the metacarpus of Landon, and I wish to emphasize here again that some of the discrepancies in the diagnosis of pure myxoma, enchondroma, *ostitis fibrosa* and giant-cell tumors may be due to the fact that different pathologists interpret the same pictures differently. In many of the bone cysts which I have examined, there have been typical giant-cell areas, and in many of the giant-cell tumors, tissue identical with *ostitis fibrosa* in cysts. Then, again, in bone cysts we may find islands of cartilage. Myxomatous tissue is not unlike *ostitis fibrosa*. Then, again, when we have a cyst, there may be little for examination, except the tissue between the bone lamellæ of the bone shell.

As far as tumors of the phalanges are concerned, I know from personal observation that cures may be accomplished by curetting in the pure myxoma and *ostitis fibrosa*, but I have had no personal experience with giant-cell tumors. From our experience with this tumor in other bones, I think we would be justified in trying curetting first.

However, Sievers's removal of the entire phalanx, with transplantation of a similar bone from the toe, has demonstrated the excellent functional result one may expect if such an operation is indicated.

Müller,³ whom I reviewed, was unable to find any medullary tumors of the phalanges. Sievers calls attention to this in his article.

BENIGN AND MALIGNANT (?) GIANT-CELL (?) SARCOMA. I only use these terms as a side-heading to draw special attention to the difference between the giant-cell tumor and other forms of true sarcoma arising in the marrow of long pipe bones. Unfortunately, there is considerable confusion due in the first place to terminology, and in the second place to

¹ *Archiv. f. klin. Chir.*, 1911, xciv, 241.

² *University of Pennsylvania Medical Bulletin*, September, 1906.

³ *PROGRESSIVE MEDICINE*, December, 1905, p. 262.

calling all sarcomas of bone containing giant-cells *giant-cell sarcoma*. This phase of the subject is best presented by Mathew J. Stewart,¹ Clinical Pathologist to the Leeds General Infirmary. The title of his excellent contribution is: Observations on Myeloid Sarcoma, With an Analysis of Fifty Cases.

Stewart uses the word giant-cell sarcoma to include all sarcomas in which there are many giant cells. He divides them into two groups: one, the myeloid sarcomas, or the myelomata of other authors, and the other, malignant giant-cell sarcomas. But he admits that the majority of the malignant giant-cell sarcomas might be called mixed-cell sarcomas.

Stewart has apparently given a great deal of attention to this matter, but I have felt, from the studies of the literature and from a most careful clinical and pathological investigation of now almost 200 bone lesions, that it will simplify the problem to confine the term giant cell to the distinctly benign type of tumor known in the literature as giant-cell sarcoma, or myeloid sarcoma. I think it would be a mistake to have a group malignant giant-cell sarcomas. These can be easily classified under sarcoma of bone, periosteal or medullary, and according to the different types of cells. In a very long experience, I have never seen among the sarcomas of bone, any cases in which, in the tumor, giant cells predominated in the picture as in the giant-cell tumor, and, as a rule, the giant cells present were of a different type. The separation of these tumors microscopically has not been difficult. As a rule, it is not difficult in the gross, but there are some very malignant bone tumors which may have the hemorrhagic granulation-tissue-like appearance of the giant-cell tumor. The Germans apparently employ the term *myeloid* for the benign giant-cell tumor, while the French and a number of American authors employ the word *myeloma* for the myeloid or giant-cell tumor. Bland-Sutton calls them myeloma, and says they do not give metastasis, and that they differ from sarcomas. He therefore describes the benign giant-cell tumor. Eve, however (quoted by Stewart), expresses the opinion that myelomas differ in malignancy. Undoubtedly, he is mixing together the two types of tumors which should be separated. Even Stewart is rather suspicious of some of the myeloid sarcomas or giant-cell tumors, and he sees no reason why occasionally there should not be a sarcomatous transformation with metastasis. Adami favors this view; Sims Woodhead looks upon the giant-cell tumor as a spindle-cell sarcoma containing giant cells. Maybury is quite convinced that he has some cases of giant-cell sarcoma which have killed by metastasis.

Stewart pictures a photomicrograph of a benign giant-cell tumor in contrast to a malignant giant-cell sarcoma. I am sorry the illustrations are not good enough for reproduction, but I would not call his malignant

¹ Lancet, November 28, 1914.

giant-cell sarcoma *giant cell* at all. It is a fully developed and apparently very malignant mixed-cell sarcoma.

While Stewart was studying his benign giant-cell sarcomas, he also looked over the material of other sarcomas of bone, and while he was able to find 50 examples of the benign or myeloid sarcoma, he picked out 5 malignant giant-cell sarcomas. Among the benign, 35 were situated on the jaw; among the malignant, 1; among the benign there were 11 examples in the long pipe bones and 4 in other bones. In the 4 malignant cases, 2 were at the lower end of the femur, and 2 in the upper end of the tibia. All of these 5 cases were radically treated, those on the limbs by amputation. Death took place in every case in from six months to three years from metastasis to the lung without local recurrence.

I would urge against the employment of the term malignant giant-cell sarcoma. It is of the greatest importance to differentiate between the different types of marrow tumors, because, as a rule, the operative treatment varies. Stewart apparently had an opportunity to examine the microscopic nodules in one case of lung metastasis, but he does not say whether he found giant cells of the type observed in the giant-cell tumor.

Stewart, after his investigation, agrees with the position I have taken in the reviews in *PROGRESSIVE MEDICINE*—that the myeloid sarcoma or giant-cell tumor should be recognized as such and subjected to conservative treatment first, curetting if possible, with resection for second choice, and amputation as a last resort.

MULTIPLE GIANT-CELL TUMORS OF BONE. Except for the more malignant periosteal and marrow sarcomas, the majority of bone lesions which appear as a single focus may also be observed as a multiple lesion. Not infrequently the multiple bone lesion may appear clinically with symptoms referred to a single focus only. In the first case of multiple myeloma which I had the opportunity to observe, there were no symptoms except swelling of the outer third of the clavicle, and no signs of a multiple bone lesion at the time of the first observation beyond Bence-Jones bodies in the urine. Later, the x-ray revealed foci in many other bones, and the autopsy confirmed these findings.

I wish to emphasize this point. Pain and tenderness in the region of a bone or joint should suggest an x-ray study. The finding of a single bone lesion, whether of the periosteum or marrow, is an indication for further x-ray studies.

I am so convinced of the importance and the necessity of taking x-rays of a number of bones that it is my opinion that the röntgenologist or the hospital should allow this to be done without further charge unless the patient can afford it. I have just seen, within a few days, a case in the private ward of a great hospital where the hospital charge for each additional plate was so excessive that this individual patient could not afford it.

F. R. Haussling and H. S. Martland¹ report an interesting observation from the City Hospital in Newark, New Jersey. They summarize their first case, in which there were multiple tumors, as being identical macro- and microscopically with their second case, in which there was but a single giant-cell marrow tumor. They express the opinion that their multiple case of giant-cell tumor is unique as it represents a clinical and pathological picture never before described in the literature.

Each tumor, as stated before, was a local growth identical with all the other bone tumors, and identical with the gross and microscopic appearance of the single giant-cell lesion.

That is, this multiple giant-cell tumor is a condition analogous to multiple myeloma, multiple tuberculosis, multiple osteitis fibrosa, etc. In these multiple bone lesions, each lesion is a primary local change in the bone in which it is situated. The etiological factor may be identical for all. We know this factor in tuberculosis and in osteomyelitis, but the cause has not been discovered in multiple myeloma, giant-cell tumors and osteitis fibrosa.

I cannot agree with the authors that their observation of the multiple lesion has never before been described in the literature. They give no reference to the literature on this subject, and apparently they have not read my² article in 1910 in which I give about twenty references under the title: Multiple Lesions of Bone, Cysts, Osteitis Fibrosa and, *Giant-cell Sarcoma*. In this list there is a reference to Rehn³ who reports a case of multiple osteitis fibrosa with giant-cell tumors—a clinical and pathological picture very similar to that of Haussling and Martland. I⁴ have critically reviewed this case. Rehn, however, calls his case multiple sarcoma in osteitis deformans, yet, histologically, the tumors were all osteitis fibrosa and giant-cell tumors. His illustrations are now of greater interest than when I referred to this article in 1906, ten years ago. His Plate IX pictures the gross appearances, and Plate X the microscopic appearance.

Haussling and Martland apparently read only my⁵ contribution on giant-cell tumors. This was distinctly supplementary to my first paper written in 1910, but on page 465 I referred to my previous article. In my second article, I was interested only in the examples of single tumors and in the possibility of a cure by curetting.

These authors also make reference to PROGRESSIVE MEDICINE, for December, 1913, but apparently failed to read what I had to say on page 290 on multiple osteitis fibrosa.

Haussling and Martland's Case of Multiple Giant-cell Tumor. The patient was a female, aged twenty-five; observation in June, 1915.

¹ Annals of Surgery, 1916, lxiii, 454.

² Ibid., lii, 185.

³ Archiv f. klin. Chir., 1904, lxxiv, 426.

⁴ PROGRESSIVE MEDICINE, December, 1906, p. 226.

⁵ Transactions of the American Surgical Association, 1912, p. 503.

The disease began with enlargement of the right upper jaw in August, 1914, ten months before admission to the hospital, and six months after considerable hemorrhage following a miscarriage. Two months after swelling of the jaw, there was a fracture of the right femur, which was treated in the City Hospital, but there is no note that an *x*-ray was taken either of the fracture or of the swelling of the jaw. This would be quite interesting, because without much doubt the bone lesion was present at that time. She left the hospital with union and no deformity. We know that pathological fractures may heal. In four months she observed a swelling of the left tibia in the middle third. She was pregnant during all this time, because in May, one month before admission to the hospital, she gave birth to a healthy child. I mention this, because pregnancy and hemorrhage are beginning to be appreciated as etiological factors in certain pathological changes in the entire skeleton.

The patient came into the hospital because of dyspnea, palpitation and bone pains. The most marked feature at the examination was the presence of multiple bone tumors, varying in size from an English walnut to a hen's egg. Their distribution was as follows: Right upper jaw, left clavicle near the sternal notch, right clavicle near acromial tip, middle of left tibia, right seventh rib. In addition to these palpable tumors, the *x*-ray revealed lesions in the femur, both fibulae, and a little later in the right humerus and pelvis. In the *x*-ray, these tumors belong to the group in which a bone shell is preserved about the marrow focus producing expansion. Bone cysts, giant-cell tumors and multiple myeloma in the great majority of cases are the lesions producing such an *x*-ray picture, but there are exceptions. The *x*-ray of the clavicle in this case shows less preservation of the bone shell and reminds me more of the picture in my observation of multiple myeloma in which the clavicle was the site of the first lesion.

In this interesting observation of Haussling and Martland, no Bence-Jones bodies were found in the urine, the Wassermann was negative, the blood showed a mild secondary anemia.

About three weeks after observation, the focus in the left tibia was explored. They describe the red granulation tissue and the free bleeding when it was curetted. They picture the *x*-ray of the expansive tumor of the left fibula and give a very good photomicrograph of the microscopic appearance. From the latter we must agree with their diagnosis of a giant-cell tumor.

The unique feature of the case, the one that should be emphasized, is that within two months they performed a second operation, curetting out the other marrow lesions. In all of the wounds, the cavity was swabbed out with pure carbolic acid followed by alcohol, and the wounds closed. Then they describe the smooth periosteum and unbroken bone shell and that each tumor was composed of red granulation tissue.

In my personal experience, and in the review of the literature, I know

of no similar observation in which all the foci have been attacked in this manner, and I think we should congratulate the authors upon the courage of their convictions and upon the most satisfactory result in their case. In November of 1915, three months after the second operation, the lesion in the lower right femur was explored. I am particularly interested in the brief sentence describing the tumor here: "This tumor mass proved to be quite cystic with very little of the characteristic tissue in its wall." Here we have, therefore, at least one lesion that was cystic and in which the giant-cell tumor did not predominate.

I have just re-read Rehn's original article, and I think we can recognize the analogy in the two observations.

Metastatic Tumors of Bone. Risley,¹ of Boston, after an investigation of this subject and the review of some 15 contributions, gives the following summary:

1. Metastasis takes place probably by centrifugal spread along the lymphatic plexus of the deep fascia in most cases.

2. Bone metastases occur almost entirely in the areas of the body subject also to skin nodule metastases, *i. e.*, everywhere proximal to the elbow- and knee-joints. Bones distal to these joints are very rarely involved.

3. Metastases are more common after cancer of the breast than any other organ, the prostate and thyroid being the next most common. (Hypernephroma of the kidney is not considered in this series.)

4. The liability of a bone to cancerous invasion increases with its proximity to the site of the primary focus. Thus the sternum and ribs are affected about equally and more frequently than any other bones. The spine, femur, humerus, pelvic and cranial bones come next.

5. The character of the secondary lesion always corresponds to that of the primary growth.

6. The frequency after cancer of the prostate may be as high as 25 per cent.

7. The vertebræ are the favorite seats of attack in scirrhus of the breast.

8. The percentage of vertebral metastases is nearly 25.

9. Spontaneous fracture is present in about 24 per cent.

10. Pain is the only characteristic symptom.

11. Visible or palpable tumor is rare, while spontaneous fracture is quite common.

12. We may set down the following points as diagnostic aids: Any fracture of a long bone occurring as a result of a trivial injury should immediately suggest the possibility of metastases and lead to careful search for the primary newgrowth. In all cases of painful paraplegia, a neoplasm should be suspected.

¹ Boston Medical and Surgical Journal, April 22, 1915, p. 584.

A diagnosis of primary bone tumors should never be made without very careful examination of the abdomen, mammary glands, prostate, and thyroid for malignancy. It is rare that careful search will fail to reveal the primary focus.

To supplement Risley's review, I would refer to the splendid article of Scudder¹ who reports cases of metastases to bone from hypernephroma, with illustrations and the literature. Since then I have found no further references to this subject in the literature.

In the contribution by Hawley,² there are three excellent x-ray pictures showing the bone tumors metastatic from cancer of the breast, and he also reproduces some illustrations from Kaufmann showing the picture of osteoplastic "carcinose" (Figs. 86, 87 and 88).

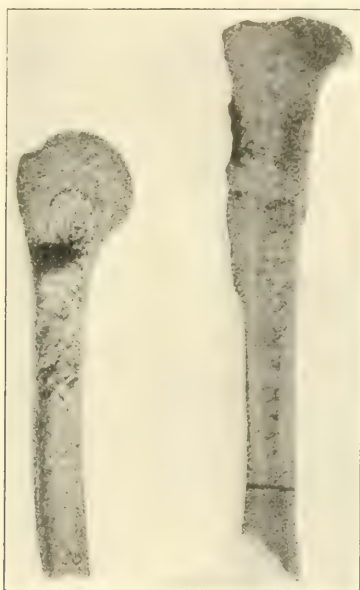


FIG. 86.—Osteoplastic "carcinose." (Hawley, after Kaufmann.)

I have operated only once for a metastatic bone tumor. In this case I amputated the right arm at the shoulder on account of the intense pain associated with the carcinoma of the shaft of the humerus. Later, I did the complete operation for cancer of the left breast. The patient was comfortable and free from symptoms for over two years. Hawley mentions this case.

Recently, Dr. Miles Porter, of Fort Wayne, resected the upper end of the femur for a carcinoma of the bone metastatic from a tumor of the breast. The patient was incapacitated and in pain because of a patho-

¹ *Annals of Surgery*, 1906, xlv, 851.

² *Ibid.*, 1910, li, 636.

logic fracture. The operation relieved the pain, and the patient was able to be up and about for the few months before she died of internal metastasis.

The most distressing side of metastatic carcinoma of bone is seen in the cases of involvement of the vertebræ. Pain is intense. In some cases there is moderate relief from absolute rest in bed. However, in one of my observations, the woman lived almost eight months—bed-ridden and in continuous agony. Paraplegia is apparently the exception, even with extensive metastases to the vertebræ. On the other

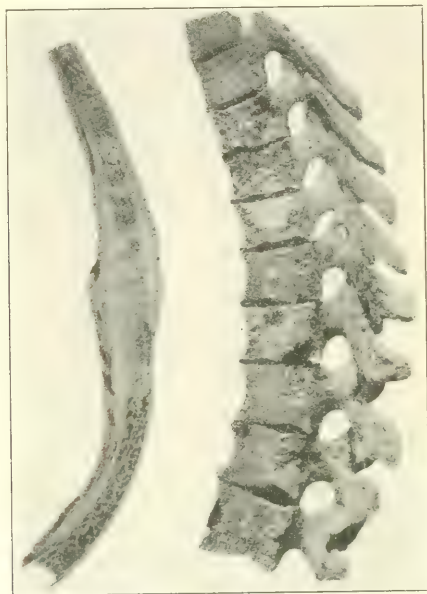


FIG. 87

FIG. 88

FIG. 87.—Longitudinal section through a carcinomatous rib. In this case metastases also in the pelvis, vertebræ, right femur, and right humerus.

FIG. 88.—Part osteolastic, part osteoplastic "carcinose" of the vertebræ—fifth dorsal to second lumbar. (Hawley after Kaufmann.)

hand, we may observe cases with extensive bone metastases to ribs and vertebræ without any symptoms. Pathological fracture does not always occur, perhaps due to the fact that the cancer cells excite new bone formation. In sarcoma, pathological fracture is the rule after the tumor has reached a certain growth.

I have observed one case of metastasis to the tibia and one to a phalanx from cancer of the prostate. I have never seen skin metastases from cancer of the prostate or thyroid. Skin metastases are not infrequent from cancer of the stomach, but bone metastases are rare.

The note by Risley that spontaneous fractures occur frequently is

probably due to the fact that his statistics are based on hospital cases, while mine include all cases. I was surprised to find the frequency of bone metastases when we thoroughly investigated the results in cancer of the breast and took routine *x*-rays when the patients complained of pain. The longer they live after operation, the greater the probability of bone metastasis.

Thyroid Tumors of Bone. In *PROGRESSIVE MEDICINE* for 1899, I called attention to the fact that single and multiple thyroid tumors had been observed in the bone, some from distinctly malignant neoplasms of the thyroid, other from thyroid tumors which microscopically were benign adenomas. At that time I reviewed the article by Honsell.¹

It is very interesting to find that J. P. Kanoky,² in reporting this one observation, apparently brings the literature up to date. The case reported by him was first observed by Zwart, of Kansas City. The unusual features are: A goitre treated by injections in 1903; the excision of the goitre in 1905; it proved to be a benign adenoma of the right lobe. The patient remained well until 1910 and then observed the pulsating tumor on the left side of the skull. An attempt at operation, within three months after the tumor was first observed, was discontinued on account of hemorrhage. Two years later, exophthalmos developed, with increase in size of the pulsating tumor illustrated by the author in photographs and *x*-ray. In January, 1913, the patient died after ligation of the common carotid artery, about three years after the onset of the tumor in the skull and ten years after the injections into the goitre. The microscopic study of the tumor, removed after death, showed benign thyroid tissue and no evidence of malignancy. The patient apparently did not present thyreotoxic symptoms.

The author also gives an excellent resumé of the literature and a brief summary of a number of cases, among them there are quite a few pulsating bone tumors. Personally, I have observed but one pulsating tumor—a giant-cell tumor.

Kanoky overlooked a very excellent article by Karl Kolb³ who gives literature not noted by Kanoky, while the latter's article contains references not given by Kolb.

Kolb finds that the majority of bone tumors appear in the skull or spine first. The long pipe bones are involved less frequently. In a number of cases, there is no evidence of a thyroid tumor and no history of thyroidectomy. At autopsy, the lungs usually show metastatic nodules, although before death there may be no physical signs or symptoms of such. The metastatic tumors as a rule grow slowly, and recurrence after operation takes place slowly. Both, Kanoky and Kolb over-

¹ Beitr. z. klin. Chir., 1899, xxiv, 112.

² Surgery, Gynecology and Obstetrics, 1916, xxii, 679.

³ Beitr. z. klin. Chir., 1912, lxxxii, 331.

look the report of Guibé¹ whose case is interesting because it was a solitary thyroid tumor occupying the outer third of the clavicle and successfully removed.

Hemorrhagic Cystic Sarcoma (Bone Aneurism). I discussed this subject first in *PROGRESSIVE MEDICINE*, December, 1913, p. 298, giving the literature and my personal experience with 5 cases. My last observation described there and illustrated in Fig. 68 and 69, is apparently well now more than three years since the amputation. But one of my² previously reported cases was free from recurrence almost three years after a shoulder-joint amputation. This type of tumor may also be observed in the soft parts, and here may be mistaken for a hematoma. When the hemorrhage is excessive, the narrow zone of tumor tissue may not be seen in the gross. I remember some two years ago performing a shoulder girdle amputation for a recurrent tumor in the region of the scapula after resection of the upper half of the humerus for a tumor of this kind. When the specimen reached the laboratory, they could find nothing but the hematoma, and greatly feared that an unnecessary amputation had been performed. I, however, was able to demonstrate tumor tissue in the wall of the hematoma, and the microscopic section revealed the same picture as seen in the primary tumor of the humerus. The case reported by C. E. Royce,³ Pathologist of the University of Iowa, is interesting, because the tumor pulsated and the diagnosis of sarcoma was made from the typical cells found in the aspirated blood. As far as I know, this is the first case of sarcoma of this type diagnosed in this way, at least I have met with no similar example in the literature. I have had one of my own.

Royce allowed the aspirated blood to stand over night. Then the blood clot was hardened in 10 per cent. formalin; it was later imbedded in paraffin and cut. The excellent histological picture is shown in Fig. 89. The patient was aged nineteen; the pain and swelling of the right shoulder had been present four years and had begun after a trauma. The growth had been slow. Fig. 90 shows the tremendous destruction of the scapula.

These hemorrhagic cystic sarcomas, wherever they may appear, are rather remarkable tumors, and those appearing in the marrow of bone are quite different from the usual malignant sarcomas in that the duration of the disease is longer and a bone shell may be preserved. In one of my cases there had been symptoms—pain and swelling in the region of the ankle—for twenty-five years, sufficiently severe to confine him to bed only fourteen months. The bone shell was preserved in this case. Perhaps this explains the intense pain, as the cavity was filled with blood under tension. In the second case there had been pain in the region of

¹ Bull. et Mém. de la Soc. de Chir. de Paris, 1909, xxxv, 117; Centralbl. f. Chir., 1910, xxxvii, 97.

² Annals of Surgery, 1910, lii, 178, Case 2.

³ Surgery, Gynecology and Obstetrics, 1916, xxiii, 74.

the shoulder four years, but rapid swelling after an injury only six months before observation. Here the bone was almost completely destroyed, and there was a huge cavity filled with blood with a bit of the head of the

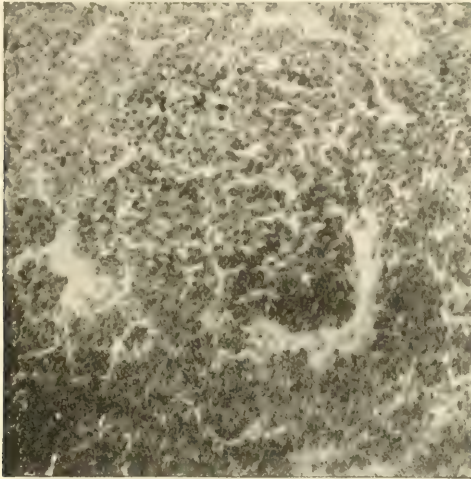


FIG. 89.—Photomicrograph showing an island of tumor cells surrounded by red blood cells. (Royce.)



FIG. 90.—Röntgenogram showing cavity formation within the tumor. (Royce.)

humerus in the upper portion and the abruptly destroyed middle third of the shaft of the humerus in its lower portion. In the third case the symptoms were of but four months' duration after a trauma. Here the

bone shell had been destroyed, there was a huge hematoma in the soft parts. These three patients died of metastases.

The fourth case reported in *PROGRESSIVE MEDICINE*¹ I remember most distinctly, because I only saw the tissue curetted from the wall of the bone cavity. This tissue looked like a giant-cell tumor. The frozen sections, however, showed a malignant round- and spindle-cell sarcoma. My colleague Dr. Finney, who operated, thought it was a giant-cell tumor, although the neoplasm itself was chiefly blood. This has been a remarkable case in its result. The patient is now living and well three years since my report and six years since operation. Coley treated this patient with his toxins, and then amputated at the shoulder-joint; he then removed a recurrent tumor in the axilla. I have examined all the sections except those of the tumor in the axilla. It is *not* a giant-cell tumor, although there are some giant cells. Stewart would probably call it a malignant giant-cell sarcoma. The remarkable thing about this case is that the patient is well, because before amputation there was a number of curetings. The fifth case I have just mentioned is interesting, because similar to the majority of the others there was a long history. During eighteen months, the patient, after careful investigation and x-ray studies, was treated for chronic arthritis of the knee. I found the tumor only after exploration. I have just seen what, I think, may prove the sixth case, and I am beginning to feel suspicious of bone shadows resembling bone cysts or the giant-cell tumors in older people complaining of much pain and tenderness and having a clinical picture like arthritis. From this limited experience, pain and tenderness are greater in the central hemorrhagic cystic sarcoma than in the giant-cell tumor or bone cyst.

I am sorry that Royce did not have an opportunity to see his tumor and to describe its gross features.

I have just ascertained that the fourth case of bone aneurism of my series, referred to Dr. Coley² for treatment with toxins, has been reported by him.

SARCOMA OF BONE AND TRAUMA. Finkelnburg³ relates the following case, from which he concludes that trauma was the etiological factor in the development of a sarcoma: A soldier, aged nineteen, was thrown to the ground, contusing the right thigh on a railroad rail; there was immediate swelling and ecchymosis; the soldier was able, however, to return to the trenches after three days' rest; at the end of four weeks there was sufficient pain to bring him back to the hospital. An x-ray, five weeks after the injury revealed a sarcoma of the femur. The thigh was amputated, but the patient died of lung metastasis.

¹ Loc. cit.

² *Annals of Surgery*, 1914, lx, 561.

³ *Deutsche med. Wchnschr.*, 1915, xli, 1561; review in *Surgery, Gynecology and Obstetrics*, 1916, xxii, abstr. p. 389.

Finkelburg reasons that the trauma was a severe one; the tumor developed at the site of the trauma; if sarcoma had been present at the time of the injury there would probably have been a fracture, or the growth of the tumor would have prevented the patient from returning to work. The trauma excited growth in embryonic rests.

Bone Transplantation. R. Sievers¹ is interested chiefly in the fate of a transplant of an entire bone with its cartilage intact at both ends. He writes that we are familiar, both experimentally and clinically, with the fate of partial transplants in all of which the marrow cavity has been exposed by longitudinal or horizontal section. But with regard to the fate of the whole-bone transplant, there is less experimental and clinical experience. Yet, in 1908, Lexer substituted the phalanx of the toe for one of the finger, because the latter was the seat of an enchondroma. Wolff, in 1910, performed a somewhat similar substitution for tuberculosis. Goebel's transplant was similar to Lexer's.



FIG. 91.—(Sievers.)

Sievers performed a similar transplantation for a tumor in the mid-phalanx of the ring finger which he looked upon as a cystic giant-cell sarcoma. To restore the toe from which he removed the phalanx, he transplanted a piece of tibia. In both instances, good function remained.

When one must remove a phalanx or metacarpus, we now have a method of substitution which will restore function. I am, however, not convinced that after the removal of a phalanx or metacarpus, it is really necessary to transplant a whole bone with its cartilage. I am inclined to think a tibial partial transplant could be cut exactly to the required size and that transplanted fascia could be substituted for cartilage. But I have as yet no cases to prove the point.

In his case he also transplanted the joint capsule, but seems to think that he would not do this again, because he attributes a great deal of the

¹ Beitr. z. klin. Chir., 1913, lxxxv, 1.

swelling and edema that occurred in the finger after operation to the presence of capsular tissue. Fig. 91 is an x-ray of the finger with its



FIG. 92.—(Sievers.)



FIG. 93.—(Sievers.)

transplant and Fig. 92 of the toe with its transplant, while Figs. 93, 94, 95 and 96 picture the hand and foot.

I wish to emphasize this case here, because my observation teaches me that the younger groups of surgeon in out-patient departments are apparently missing many opportunities not only for the investigation

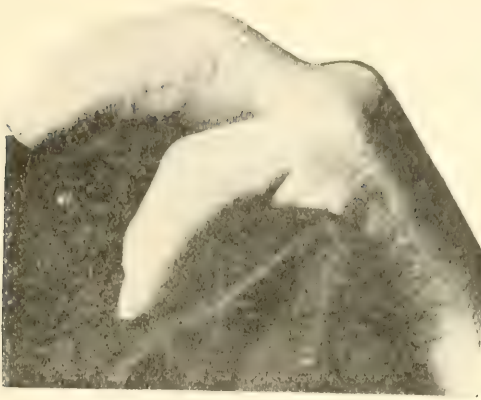


FIG. 94.—(Sievers.)



FIG. 95.—(Sievers.)



FIG. 96.—(Sievers.)

of tumors in the region of the fingers, but for operative measures which have for their object not only the cure of the disease, but the restoration of function of hand and foot. Too many fingers and toes are sacrificed, as this is a quick and simple operation, while operations similar to those just reported demand a knowledge of the literature, and willingness to sacrifice time for the benefit of the patient. As I recollect the literature on diseases of the fingers and toes and on conservative operations, I cannot at the present moment recollect any from American literature, while I have reviewed in *PROGRESSIVE MEDICINE* many from German sources.

TRANSPLANTATION OF FIBULA FOR HUMERUS. Elsberg¹ resected the head and two inches of the shaft of the humerus; into the defect he transplanted five inches of the upper end of the fibula; the head of the fibula was placed into the glenoid cavity and the other end was wedged into the shaft of the humerus. The operator lays much stress on the fact that he isolated the tendons of the intraspinous and teres minor, and sutured the tendons to the upper end of the fibula. The patient, an oculist, was able to use this arm to operate within five and one-half months.

My own experience teaches me that this is the best method when one must resect portions of the humerus. The point of tendon suture mentioned by Elsberg should be borne in mind. It is usually not done. I may be able at a later time to ascertain whether it is really necessary. The cases with which I am familiar have good function for ordinary things, but none of them are surgeons. It seems to me this transplantation of the fibula, even if there is one horizontal cut exposing the marrow cavity, is practically the same as the transplantation of a small pipe bone intact. Apparently, Sievers² did not look upon cases of this kind as evidence suggesting that such implants would live. The fibula has been used for transplants more than any other bone; the tibia has been employed most to supply chips of various sizes.

¹ *Annals of Surgery*, 1916, lxiv, 106.

² *Loc. cit.*

PRACTICAL THERAPEUTIC REFERENDUM.

By H. R. M. LANDIS, M.D.

Adrenalin. During the recent epidemic of *acute poliomyelitis* considerable discussion has been aroused as to the value of adrenalin advised by Meltzer. In a recent article, Meltzer¹ has replied to his critics and gives his reasons for advocating this method of treatment. He points out that his suggestion was not an idle one but is one which is based on physiological and experimental facts.

Meltzer's procedure is as follows: As soon as the diagnosis of poliomyelitis is established, 2 c.c. of 1 to 1000 solution of adrenalin should be injected into the spinal canal every four to six hours. Before the first injection is given, a fairly large quantity of spinal fluid should be withdrawn, the quantity being in proportion to the pressure prevailing in the spinal canal. The subsequent injections should be made without regard to the presence or absence of spinal fluid. Unless the pressure appears to be very high, he advises that in advanced cases not much spinal fluid be withdrawn, because at this stage the spinal fluid may already contain some useful antibodies. All injections should be washed in with 2 c.c. of normal salt solution, but, if no spinal fluid is present, the adrenalin should be washed in with at least 5 or 6 c.c. of salt solution; on the pressure of fluid in the spinal canal the adrenalin will more readily spread over the cord. In serious cases the quantity of adrenalin administered may be as much as 3 c.c. to each injection. In cases in which the encephalitic symptoms are predominant, however, greater care should be exercised with reference to the quantity of the injected adrenalin; it should be used in proportion to the exciting effect which the injections may produce. In some of his experimental work, Meltzer found that adrenalin was often destroyed when mixed with human spinal fluid. He prefers therefore that the injections should be given oftener, at least every four hours when possible. The injections should be continued until four or five days after all paralysis has disappeared, or at least until no further reduction in the extent of the paralysis has taken place.

In addition to the use of adrenalin, Meltzer believes that oxygen should be administered under pressure in respiratory rhythm. He has devised an apparatus for this purpose which permits the oxygen to be forced into the mouth under pressure. As a rule, the patient adapts his own respiration to the rhythm of the apparatus.

¹ New York Medical Journal, August 19, 1916.

As the result of experimental work, E. D. Brown¹ states that his observations tend to show that when *adrenalin* is perfused through the cerebral circulation, it may, in a certain proportion of cases, cause a slowing of the heart, and that this slowing is, at least in part, due to direct stimulation of the vagus centre. There is also some evidence which strongly suggests the probability that the drug also stimulates the vasomotor center. The effect on the respiratory center is variable.

Muto² has studied the *action of adrenalin on the secretion of sweat*. In a number of animals in which he had injected adrenalin intravenously or subcutaneously, the sweating was marked. In one horse under the influence of adrenalin, the total amount of sweat collected amounted to 1230 c.c. Muto undertook the research in order to determine whether or not the sweat glands are innervated by the sympathetic system exclusively. His results indicate that both the sympathetic and parasympathetic systems are involved. The latter predominate in man, cats, and cattle, while the former is chiefly involved in horses and sheep.

Antitoxic Sera. ANTIDIPHTHERITIC SERUM. During the past few years attention has been called in this review to the increasing number of physicians who advocate the *intravenous* or *intramuscular method* of administering antitoxin in severe cases of diphtheria. Dupaquier³ reports 32 cases, 21 of which were of a severe type. Eight of the 21 severe cases died. He believes that the intravenous method is the one of choice. The temperature drops to normal in from twelve to twenty-four hours, the membrane disappears quickly, the symptoms abate more quickly than when the other methods are employed, complications are fewer and the convalescence is shortened. Another factor in favor of this method is that the number of "carriers" is lessened.

Dupaquier states that the intravenous method also results in a great saving of serum, as the amount used is far less than in the other methods. In most of his cases, an initial dose of 10,000 units was all that was given. He suggests that serum used intravenously be made of a greater dilution, if possible a high dilution of dry globulins, not a concentrated solution, and that it should be clear, not cloudy. The serum should be warmed and administered at the temperature of the body. Finally, he recommends that the gravity method should be used instead of the hand-syringe "push method."

Dupaquier recommends that the injection should not be made at once, in those walking into the hospital, or after exertion of any kind. There should be a rest of at least one hour in bed before the injection is made.

Woody,⁴ who has previously advocated the use of *intramuscular injections*, has again reported on the method. The advantages over the

¹ Journal of Pharmacology and Experimental Therapeutics, April, 1916.

² Abstract, Journal of the American Medical Association, May 27, 1916.

³ New Orleans Medical and Surgical Journal, September, 1915.

⁴ Pennsylvania Medical Journal, December, 1915.

subcutaneous method are: (1) More rapid absorption, quicker therapeutic action; (2) need for a smaller dose of antitoxin to produce identical effect in the same patient, and, therefore, (3) economy in use of antitoxin; (4) intramuscular injections are less painful; (5) they are less liable to be followed by abscesses; (6) the technic is quite as simple as that of subcutaneous injections; (7) there are no unfavorable results of the intramuscular injection which might be considered as contra-indications to its use.

The injection is made in the middle of the outer aspect of the thigh. The skin receives two coats of a 5 per cent. tincture of iodine and the needle is plunged well into the muscle. After the injection is made, the skin is sponged with alcohol and a sterile gauze pad or collodion dressing applied.

In a series of 600 cases treated by this method, Woody states that the initial dose varied from 3300 to 100,000 units and rarely was it necessary to give a second dose. He states that the bulk of antitoxin and the expense are cut in half. Of the 600 cases treated, 33 died, a mortality of but 5.5 per cent. In the entire series the location of the process was as follows: Laryngeal, 89 cases; tonsillar, 298 cases; faucial, 24 cases; nasal, 30 cases; tonsillar and faucial, 40 cases; nasal and laryngeal, 2 cases; tonsillar and nasal, 38 cases; tonsillar, faucial and nasal, 3 cases; tonsillar, faucial and laryngeal, 1 case.

Kossel¹ reviews the *changes* which have been wrought by diphtheria antitoxin during the past twenty-five years. In April, 1893, were published the first cases of antitoxin-treated diphtheritic children. At this time the mortality from diphtheria in German cities of over 15,000 inhabitants ranged from 85 to 130 per 100,000 inhabitants. After diphtheria antitoxin came into clinical use, in 1895, the mortality dropped to 50, and since 1899 has never reached 30, keeping on a level line between 21 and 29.

Since the introduction of the *Schick reaction* it is now possible to determine cases in need of immunization and those who possess a natural immunity. The practical use of the test is illustrated by an experience related by Veeder.² A child was admitted to the hospital with negative cultures for diphtheria at the time it entered. Several weeks later it developed clinical diphtheria, to which some 26 children were exposed to a greater or lesser degree. A diphtheria toxin test ("Schick test") was made, and 8 reacted positively and 18 negatively. No further attention was paid to the 18 negative cases, but the 8 positive cases were passively immunized by injecting antitoxin and no further cases of diphtheria developed. Thus the cost of immunizing 18 children, together with the unpleasant skin reactions and sensitization which so frequently follows

¹ Deutsch. med. Wchnschr., December 2, 1915.

² International Clinics, vol. iii, 26th series.

injections of antitoxin, was avoided in over two-thirds of the cases. The same procedure may be followed in private families and in orphanages.

Diphtheria Immunization. In their paper entitled "Active Immunization with Diphtheria Toxin-Antitoxin and with Toxin-Antitoxin combined with Diphtheria Bacilli," Park and Zingher¹ draw the following conclusions:

1. Individuals who, before treatment, give a negative Schick reaction are immune probably for life and, therefore, it is not necessary to inject them, when exposed, either with antitoxin or toxin-antitoxin.

2. Those who give a positive Schick reaction and are exposed to diphtheria and in immediate danger should receive either antitoxin alone or, if a longer protection is desired, both antitoxin and toxin-antitoxin.

3. For the general prophylaxis against diphtheria in schools and communities, excluding immediate contacts, a mixture of toxin-antitoxin alone (from 85 to 90 per cent. of the L + dose of toxin to each unit of antitoxin) or toxin-antitoxin plus vaccine of killed diphtheria bacilli is recommended. The dose is 1 c.c. of toxin-antitoxin and 1,000,000,000 bacteria injected subcutaneously and repeated three times at intervals of six or seven days. Sufficient time has not as yet elapsed to judge the value of adding the injections of the bacilli to the toxin-antitoxin.

4. The early and the late results of active immunization should be determined with the Schick test. Early results are those obtained by the application of the test within four weeks, and late results from four months to two years after the immunizing injections.

ANTITETANIC SERUM. While tetanus antitoxin has not fulfilled the hopes for a cure which were at first claimed for it, Kossel² states that this war has demonstrated most emphatically its value in prevention. This statement is amply justified by reports made during the first year of the war and by those recorded for the past year. Wolf³ states that, following the decree of the German authorities that every wounded soldier be given a preventive injection of tetanus antitoxin, the number of cases of tetanus dropped off to almost zero. The facts, as related by Wolf, indicate that the preventive injections are an almost certain protection against tetanus and that the injection need not be made at once. It may be delayed till the following day without detracting from its efficacy.

Extraordinarily good results are reported by Kümmell.⁴ In an inquiry which he made in various German hospitals as to the occurrence of tetanus during the ten or eleven months since the wounded have been given prophylactic injections of tetanus antitoxin, he obtained the following facts: In one hospital, that previously had had numerous cases of tetanus, there was only one instance among 700 wounded and in this

¹ Journal of the American Medical Association, 1915, lxx, 2216.

² Deutsch. med. Wchnschr., December, 1915.

³ München. med. Wchnschr., September 28, 1915.

⁴ Berlin. klin. Wchnschr., April 17, 1916.

case the man, through a mistake, had failed to receive an injection. At another place, among 1555 severely wounded men, only one case developed, and that ended in recovery. During the period in question, Kimmell was able to learn of but 42 cases known in army circles, although the conditions were essentially the same as during the period prior to the use of routine injections. He emphasizes the fact that the protection given by the prophylactic injection lasts for only about fifteen days, and, if the wound is much contaminated, only about a week's protection can be counted on. If any operative interference is contemplated, another injection should be given even if a comparatively long interval has elapsed since the first one. This point is also emphasized by MacConkey.¹ He states that when an operation is proposed in wounded who may have been infected with tetanus bacilli, it is imperative to bear in mind that there may be toxin circulating in the body. For this reason a large prophylactic injection is necessary, and it should be given in such a way as to ensure that there is no free toxin in the blood at the time of the operation or for sometime after. MacConkey believes that those cases of tetanus which develop some weeks after the receipt of an injury may be due to the reactivation of a quiescent focus by too early or too energetic active or passive movement. A remarkable case of tardy or delayed tetanus is reported by Deutschlaender.² The case was that of a young man who developed fatal tetanus five months after a grenade wound of the chest. He had been given tetanus antitoxin at the time. One hundred and forty days after the infliction of the wound, he collapsed after a change of the dressings. The symptoms of tetanus quickly developed and a fatal result occurred in twenty-four hours. In this case the germs were evidently encapsulated, and, as the result of changing the dressings, some disturbance was produced which enabled the germs to enter the circulation.

MacConkey³ adds to the favorable testimony regarding the prophylactic use of the antitoxin. His experience has been gained through the use of from 500 to 1000 United States army units of tetanus antitoxin.

Robertson⁴ states that in the great majority of cases the subcutaneous injection of 20 units of tetanus antitoxin immediately after an injury will certainly prevent the occurrence of tetanus. He believes that the delay of a few hours in making the injection may mean the loss of life. Wolf,⁵ it will be recalled, states that the injection may be delayed until the following day. We incline to Robertson's advice to inject early. Delay may not be serious in those with a long incubation period, but, in the acute cases, the sooner the injection is made the better. Robertson advises the immediate application to wounds of dried antitoxin tampons moistened by clean fluid as a temporary measure, in cases in which the

¹ British Medical Journal, December 11, 1915.

² Deutsch. med. Wchnschr., December 2, 1915.

⁴ American Journal of the Medical Sciences, May, 1916.

³ Loc. cit.

⁵ Loc. cit.

injection cannot readily be made. This method is to be used only when other measures are not immediately feasible. He cautions against secondary surgical operations until a second injection of antitoxin is made.

Kocher¹ emphasizes that the main point in the treatment of tetanus is to gain time, tiding the patient along until antibodies are produced to neutralize the tetanus antitoxin. *Magnesium sulphate* is of great service during this waiting period. Instead of giving one large dose, Kocher advocates fractional doses during the twenty-four hours and continued for from six to eighteen days. This may be done without harm. He commences with the largest fraction of the dose, reaching the total dose of 1.5 gm. per 1 kilo of body weight before the close of the twenty-four hours. The severer the case, the larger the portion to be given at first. It may be advisable to inject into a vein or into the spinal canal.

Bruce² has analyzed 231 cases of tetanus treated with serum. Of this number, 98 recovered and 133 died, a mortality of 57.7 per cent. In these cases, if the symptoms developed within ten days of receiving the wound, the mortality was 66.6 per cent., if between the eleventh and twenty-fifth day, 39 per cent. It is stated that the death-rate in untreated cases is 91 per cent. in those of short incubation, and 50 per cent. in those of delayed incubation. Among the 231 cases, however, 37 are noted as having been treated with antitetanic serum before the onset of symptoms. Of these, 18 recovered and 19 died, giving a mortality of 51.3 per cent. Whatever value antitetanic serum may have in the treatment of tetanus is considered to be largely due to serum injected intrathecally. *Magnesium sulphate* seems to have been used but little in England, and without encouraging results.

Bruce sums up the treatment of tetanus as follows:

Place in a quiet, darkened room under the care of a sympathetic and capable nurse.

The best surgical treatment of the wound should be thoroughly carried out to ensure the prompt and complete removal of all septic products.

The intrathecal injection of at least 3000 units of antitetanic serum. At the same time, 10,000 to 20,000 units may be injected intravenously and subcutaneously. This procedure to be repeated as frequently as the course of the disease seems to demand.

In addition to this, the patient should receive sedative drugs, such as chloral or chloretone, in full doses.

Pribram³ advises in the treatment of the wound the radical excision of all necrotic tissue down into fresh bleeding tissue. Anything inducing a scab favors the development of tetanus.

¹ Correspondenz-Blatt f. Schweizer Aertze, October 2, 1915.

² British Medical Journal, October 23, 1915.

³ Berlin. klin. Wchnschr., August 30, 1915.

SERUM TREATMENT OF POLIOMYELITIS (INFANTILE PARALYSIS). This subject is discussed in a timely article by Flexner,¹ who briefly summarizes the work done by himself and others in regard to immune bodies in monkeys and human beings who have recovered from the disease. The impossibility of reinoculating, with the virus, those animals that had survived an attack of the disease, the detection in the blood of such protected monkeys and human beings of immunity substances capable of neutralizing the virus of poliomyelitis when the serum and the virus were brought together in a test-tube, and the discovery that the serum of monkeys actively immunized with the virus, under conditions in which all symptoms of the disease were avoided, contained similar immunity bodies, all these steps prepared the way for the therapeutic application of such immune serum to animals actively affected with the disease. Encouraging results were obtained, for it was found that the power "to neutralize the virus possessed by immune serums is exercised *in vivo* under severe experimental conditions almost as constantly as *in vitro* under relatively favorable ones." Possibly the favorable results were partly due to the early stage of the disease at which the treatment was applied, the monkeys being inoculated with the virus on one afternoon, and receiving the immune serum within eighteen to twenty-four hours later.

The further application of this treatment to man has hardly been extensively enough employed as yet to warrant any definite statements as to what should be expected from it. Netter was the first to apply the treatment to human beings, and, in a small series of 35 cases, he published results which he considered highly favorable. As immunity persists for years in those who have had the disease, it is not necessary to employ the serum of those recently recovered, though it is probable that such serum is somewhat more potent.

Flexner recommends the subdural injection by means of lumbar puncture, of from 5 to 20 c.c. of the immune human serum, repeated several times at twenty-four hour intervals, according to clinical conditions and indications. The serum should be employed in the preparalytic stages and in progressing paralytic conditions. "The conditions surrounding the injection of the serum into the meninges are identical with those observed in the analogous case of epidemic meningitis. Before each dose of serum is injected, a suitable quantity of the cerebrospinal fluid is to be withdrawn and the injections should be made slowly." The donor of the serum must, of course, be a healthy individual, and the usual clinical examination should be fortified by a Wassermann test. Flexner advocates the wider employment of the treatment where the difficult conditions surrounding the obtaining of immune human serum can be surmounted.

¹ Journal of the American Medical Association, 1916, lxvii, 583.

SERUM TREATMENT OF SCARLET FEVER. The use of fresh whole blood taken from convalescents and injected intramuscularly into individuals suffering from scarlet fever is reported on by Zingher.¹ The blood obtained from the donor may be subjected either directly, or it may be citrated previously by adding an ounce of blood to 1 c.c. of a 10 per cent. solution of sodium citrate, making the final dilution of the citrate 0.33 per cent. Zingher recommends the following muscles into which the injection may be made: The gluteal regions, the outer regions of the thighs, calves, and the triceps muscles. Four ounces of blood can easily be injected into a young child, and eight ounces into an older child or adult. Zingher has treated 14 cases of toxic scarlet fever by this method. The blood was obtained from patients who were convalescent from two to six weeks. The amount injected varied from 75 to 250 c.c., depending, to some extent, on the age of the patient. In 7 of the cases the blood was citrated. The blood mass was absorbed, without any local irritation, in all the cases except one. In this case there was a painful and tender swelling in one calf and the opposite gluteal region, which lasted for a few days.

Of the 14 cases treated, 4 died. In the remaining 10, Zingher believed there was a distinctly favorable influence on the course of the disease. There was a distinct critical drop in the temperature in cases not complicated by a streptococcus exudate or inflamed cervical lymph nodes. Zingher believes that by using larger quantities of fresh normal blood, a distinct beneficial effect on the disease may be exerted, especially by injecting from eight to ten ounces of blood, and repeating it, if necessary, in four or five days.

SERUM THERAPY IN THE TREATMENT OF TRICHINOSIS. In a preliminary communication entitled "A Study of an Epidemic of Fourteen Cases of Trichinosis with Cures by Serum Therapy," Salzer² presents a good deal of interesting material in a very small space. In regard to the effects of the administration of serum in trichinosis, he says:

The use of serum from human patients who recovered removed the eosinophilia persisting after recovery in man or animals within forty-eight hours.

The injection of normal serum had no therapeutic value in trichinosis in man or animals. The same is true of salvarsanized serum and salt solution.

In animals, the injection of convalescent serum gives an almost complete prophylactic result. Animals fed with infected meat within twenty-four hours after the administration of the serum may develop a mild form of trichinosis. Animals fed at a later period than that prove to be immune. All these experiments were controlled.

¹ New York State Journal of Medicine, March, 1916.

² Journal of the American Medical Association, 1916, lxxvii, 579.

If immune serum is mixed with infected meat and then fed, the animals do not develop trichinosis, although the ingestion of the same meat without the serum is invariably followed by the appearance of the disease.

In 2 cases of trichinosis in the very active stage of the disease, the use of immune serum proved to be of remarkable curative value. There was a decided drop in the temperature within six hours, and the abnormal temperature was entirely gone within forty-eight hours. The eosinophilia showed a considerable drop within six hours; there was then a secondary rise and then a return to the figures found in normal blood within forty-eight hours.

In twenty-four rabbits suffering from the disease experimentally produced, the immune serum had a curative effect within twenty-four hours.

SERUM SICKNESS AND ALLIED PHENOMENA. The so-called serum phenomena, such as urticaria, fever, adenitis, etc., occurred in 56.7 per cent. of patients receiving diphtheria antitoxin reported by Molchanova¹ and in 64.3 per cent. of those treated with antistreptococcus serum for scarlet fever. In those cases in which the antitoxin for diphtheria or serum for scarlet fever had been injected more than once, such phenomena were present in 100 per cent. of cases, but after a single injection complications were noted in only 47.5 per cent. of cases treated with antitoxin, and in 59.6 per cent. of scarlet fever cases. The most frequent sign was a rash in the form of urticaria, erythema multiform, measles-like, scarlatiniform or hemorrhagic. Of the rarer complications the author mentioned affections of the joints (arthralgia, synovitis), elevation of temperature, albuminuria, and edema, the last being unassociated with albuminuria casts, or increase in blood-pressure. Gastro-intestinal disorders also occurred. Cardiac collapse occurred in four cases, with one death. In regard to prevention and treatment of the serum phenomena, Molchanova found that concentrated serum gave fewer complications.

Calcium chloride (2 per cent. solution, a teaspoonful three or four times a day) did not ward off the complications. The anti-anaphylactic method of Besredka (2 c.c. of antitoxin injected intramuscularly followed in two or three hours later by the curative dose hypodermically or intramuscularly) was used in 15 cases, but without benefit in preventing complications. The latter, however, were rather mild and Molchanova warmly recommends the method.

Woody,² in reporting 600 cases treated by intramuscular injections, states that 136 (22.6 per cent.) developed serum rashes; of these, 129 were urticarial, 2 were morbilliform, and 5 were scarlatiniform. In

¹ Russkiy Vrach, vol. xiv, No. 38.

² Pennsylvania Medical Journal, December, 1915.

1000 cases treated at the Municipal Hospital of Philadelphia by the subcutaneous method, serum rashes occurred in 43.4 per cent.

Antimony. The use of antimony in the treatment of *kala-azar* is recommended by Bahadur.¹ One grain of metallic antimony is made into a thoroughly homogeneous paste with a sufficient liquid glucose in a glass mortar and then mixed with 20 c.c. of normal saline solution. This is injected into a vein. If any of the sediment is left in the syringe, it is mixed with normal saline containing 5 per cent. glucose, and then injected into a vein. This process is repeated until all of the antimony has been injected. In order to accomplish this, from 40 to 45 c.c. of normal saline are required to carry in from 1 to 1½ grains of antimony. Aside from a severe diarrhea which may last for a day or two, Bahadur has not had any serious results.

Arbutin. This is a glucoside obtained from *uva ursi* and allied species of plants. It is usually given in increasing doses. The ordinary dose is from 1 to 7 grains, but this may be increased up to 15 grains. It is excreted principally by the kidneys and has a marked sedative and tonic effect on the mucosa of the bladder. Lynch² recommends its use in the bladder disorders of the senile male. In some cases of enlarged prostate, the use of arbutin is followed by great relief of the urinary symptoms and a decrease in the size of the prostate. Waugh³ highly recommends the drug in patients suffering from vesical catarrh. Even in cases of long standing, the result of gonorrhea, good results are often obtained. The drug must be used over a long period of time in order to obtain results.

Arsenic. This drug has long enjoyed a reputation of exerting a specific action in *tuberculosis*. This view is shown to be fallacious by Arkin and Cooper.⁴ In their opinion, any favorable action the drug may have in tuberculosis is to be attributed to its effect on metabolism. In advanced cases of tuberculosis it may even be harmful. Experimentally, they found that the arsenic in the form of sodium arsenite, sodium cacodylate, atoxyl, arsacetin, and neosalvarsan, administered to tuberculous animals, is found in the liver, lungs, kidneys, blood, spleen, and tuberculous tissues (lymph nodes of guinea-pigs and eye of rabbit). There was no evidence, however, that the drug accumulated in the tuberculous tissues.

Artificial Respiration. In a very valuable contribution entitled "Resuscitation Apparatus," Henderson⁵ discusses the value of various apparatus used in resuscitation from electric shock, drowning, and asphyxiation by poisonous gases, and compares the relative value of

¹ Indian Medical Gazette, December, 1915.

² American Journal of Clinical Medicine, November, 1915.

³ Ibid., December, 1915.

⁴ Journal of Infectious Diseases, April, 1916.

⁵ Journal of the American Medical Association, 1916, lxvii, 1.

apparatus with the former pressure method of artificial respiration. While admitting the superiority of the former method when the conditions for its use are favorable, he emphasizes most particularly that the main element in success in either method is the time of application after the person has been injured. "The most important scientific point in this connection, however, is the fact that from the moment when spontaneous respiration ceases, whether by drowning, electric shock, excess of anesthesia, gas poisoning, or any other form of asphyxia, the probability of restoration by any method grows rapidly less as the minutes pass." The Resuscitation Commission (of the American Medical Association and the National Electric Light Association), after considering the matter in the light of such evidence as is available, concluded that "probably ten minutes is the extreme limit of time beyond which restoration is practically impossible." Granting the advisability of providing apparatus in those fields of work in which it can be at hand when an accident occurs, such apparatus loses its value if any length of time is lost in sending for it. The provision of such apparatus should never replace drilling in manual methods, and these should be resorted to at once if the apparatus is not immediately available. Henderson concludes as follows:

1. Universal training in the pressure manual method of artificial respiration will accomplish more for resuscitation from drowning, electric shock, and asphyxia than is possible by providing any amount of apparatus.

2. Artificial respiration with apparatus is superior to the manual method, in that the apparatus is capable of giving a normal volume of pulmonary ventilation while the manual method is not.

3. Nevertheless, the immediate application of a poor method is far more important than the application of a perfect method after a delay of even five minutes. The knowledge that apparatus is available is liable to result in a neglect of immediate manual treatment in order to have the apparatus brought from a distance.

4. Apparatus should be provided only in places in which it will be immediately available.

5. Since all that any apparatus yet invented affords is artificial respiration with air more or less enriched with oxygen, it should be of a simple type so as not to produce exaggerated ideas of its efficiency.

6. Oxygen inhalation should be used immediately in gas and smoke cases, but the apparatus employed should be such as will allow the oxygen to reach the patient's lungs in efficient concentration. Such apparatus should go with every artificial respiration device.

7. Investigation of the use of artificial respiration apparatus in asphyxia neonatorum is needed.

Atropine. The treatment of *cholera* by the addition of atropine hypodermically to the hypertonic and permanganate treatment has

further greatly reduced the death-rate in this disease, according to Rogers.¹ It appears to act by lessening shock, raising the blood-pressure, diminishing the frequency of the respiration, increasing the flow of urine, and diminishing slightly the number of intravenous injections required. The number of deaths from collapse and from pneumonia has been greatly diminished, while the total mortality in the atropine series has fallen off one-half that of the controls, and to but little more than one-sixth of the death-rate before he introduced the present system of treatment; a reduction in the mortality of a very serious specific disease by means of simple measures, based on prolonged scientific research, controlled by minute clinical observations, the study being conducted on over 1000 cases. In brief, Rogers's treatment is as follows:

On admission, give one-hundredth of a grain of atropine hypodermically and repeat it morning and evening. Take the specific gravity of the blood, the blood-pressure, and the temperature in the mouth and rectum. If the blood-pressure is not over 70 mm., or the specific gravity is 1063 or over, give an intravenous injection of sterile hypertonic saline of 3, 4, 5, or even 6 pints, in accordance with whether the specific gravity is 1063, 64, 65, or 66, and over, in male adults, and correspondingly less in females and children in proportion to their approximate weights. Unless the rectal temperature is below 99° F., the saline should never be injected at above blood heat (98° F.) for fear of producing hyperpyrexia. If the rectal temperature be 100° F. or over, the fluid should be given at a temperature between 80° and 90° F. The hypertonic solution should contain 120 grains (8 grams) of sodium chloride and 4 grains (0.4 grams) of calcium chloride. Permanganate of potash is to be given in 2-grain pills, made up with kaolin and vaselin, and preferably coated with salol or keratin, 2 pills every quarter of an hour for two to four hours, in accordance with the severity of the case, and then 2 every half hour until the stools change to green or yellow, and become comparatively small.

Barley water or plain water by the mouth in small quantities at a time (3 or 4 ounces) are to be given frequently, but no other food during the attack. Normal saline (sodium chloride, grains 90 to a pint) half a pint every two hours is to be given by the rectum until the collapse stage is passed and urine is being excreted regularly, the frequency is then to be reduced to every four hours and continued until 2 pints of urine are passed in twenty-four hours.

The fall of the blood-pressure to 70 and under, or the rise of the specific gravity of the blood to 1063 or above, are indications for a repetition of the intravenous injection, estimations being made regularly morning and evening, and at any time that the pulse tends to fall or the patient becomes restless. Here again we find the tendency to

¹ Indian Medical Gazette, January, 1916.

acidosis, which is the most essential cause of post-choleraic uremia, combated with sodium bicarbonate solution. At each repetition of the intravenous injection of hypertonic salt solution, and at the first injection in all cases admitted late with suppression of urine for twenty-four hours or more, 1 pint of the following alkaline solution is administered: Sodium chloride 60 grains and sodium bicarbonate 160 grains (2 per cent.), the ordinary hypertonic solution being continued up to the total amount indicated by the specific gravity of the blood.

If the urinary excretion is deficient in the later stages, with a blood-pressure of 100 mm. or more and a specific gravity of below 1063, but not much below the normal point of from 1056 (in Indians) to 1058 (in Europeans), 1 pint of the above solution is to be given subcutaneously or, better, intravenously, to increase the urinary flow. The alkalies in such cases should also be given by the rectum instead of normal saline.

If the blood-pressure remains persistently much below 100 mm. and the urine is deficient, give pituitrin hypodermically and caffeine sodiosalicylate in 5-grain doses by the mouth every four hours, and dry cup and foment over the kidneys repeatedly. In very young children and feeble old patients, glucose may be given in the rectal saline to support the strength.

The effect of this drug in a case of *bradycardia*, the slow pulse being apparently prominent and not paroxysmal in character, and having some obscure nervous origin, is reported by Cottin.¹ The patient was a woman, aged thirty-four years, who, since nineteen years of age, had been subject to so-called nervous crises, a gradual progressive enlargement of the thyroid gland developing about the same time. The slow pulse-rate was discovered when she was twenty-six years of age, the rate being between 45 and 55. About four years later the rate varied between 45 and 50. A condition of incomplete auriculoventricular block was discovered. Later the tracings showed a complete and permanent disassociation. Syncopal attacks which had been present previously became slightly less frequent, were of longer duration, and were accompanied by total loss of consciousness. Tracings were taken at this stage a few minutes and forty-five minutes respectively after the injection of 2 mg. of atropine sulphate. In the first tracing the ventricle was beating at the rate of 38, the auricle at 93, and the independence between the two cavities of the heart was evident and complete. In the tracing taken after forty-five minutes, no sign of block remained. The rate of contraction of both auricle and ventricle was 85; the interval P. S. had become uniform and did not exceed the normal length. The effect of the atropine was the more striking since movements, walking, fever, all of them causes which lead, as a rule, to quickening of the pulse, had always been without marked influence on the heart rhythm.

¹ Referred to in the *Therapeutic Gazette*, March, 1915.

Atropine in Gastric Disorders. In discussing the treatment of gastric diseases, Friedenwald¹ states: "That of the many remedies employed in the treatment of the various gastric disorders there is one of unusual importance, as it appears to have an almost specific effect in certain conditions. The drug is atropine, which, by depressing the vagus fibers, decreases the secretory and motor functions of the stomach." Through the researches of Eppinger and Hess, the theory has been advanced that disturbances of the autonomic nervous system (which includes all the efferent nerve fibers outside of the cerebrospinal axis excepting those supplying the voluntary muscles) lead to increased and decreased tonus or excitability, and that through this system the activity of the glands of internal secretion are regulated and controlled. According to this theory, therefore, a gastric ulcer may have as its underlying basis an increased vago-tonus, and atropine by depressing this vagus excitability decreases the possibility of gastric irritation. Clinically, it has frequently been noted that healing has been effected in obstinate cases of gastric ulcers when patients were systematically treated with atropine or belladonna.

O'chsensus² advocates the use of atropine in the treatment of *pylorospasm in children*. It has been shown in Czerny's pediatric clinic that children can bear much larger doses of atropine than adults and for this reason the drug is especially useful in pylorospasm. O'chsensus states that if the spasm is not relieved by the use of atropine, we can confidently assume that there is a congenital stenosis present. As an illustration of the amount which even a very young child can take without harmful results, he cites the case of an infant three weeks old to whom the atropine was given by mistake at each of eight daily feedings making a total of 1.2 mg., which it bore for a week without harm.

Block³ reports favorable results from the use of atropine in the treatment of *dysmenorrhea*. He gives one-hundredth of a grain of atropine sulphate two or three times daily for two days before the expected period, and continues it after the flow appears until the symptoms are relieved. In addition to the use of the atropine he keeps the bowels open and between the periods tries to improve the personal hygiene.

Benzol. Boardman⁴ believes that the use of benzol in the treatment of *leukemia* is unattended with danger if proper precautions are used. He administers the drug in freshly filled gelatin capsules, with an equal amount of olive oil. The maximum daily dose should not exceed 5 gm. During the time the drug is being taken, there should be frequent examinations made of the blood and urine. The drug should be discontinued if there is any evidence of kidney irritation or when the

¹ Therapeutic Gazette, February, 1916, referred to elsewhere.

² Deutsche med. Wchnschr., December 16, 1915.

³ American Journal of Obstetrics and Diseases of Children, December, 1915.

⁴ California State Journal of Medicine, September, 1915.

leukocytes fall to 25,000 or 20,000 per cm. The best results follow the combined use of benzol and the *x*-rays.

Bismuth. The extensive use of bismuth in *x*-ray work and in the form of bismuth paste makes it important to bear in mind that the use of this drug in large quantities is occasionally attended by symptoms of poisoning. Higgins¹ states that up to date there are on record 65 cases of poisoning, with 24 fatalities. Higgins reports a case in which poisoning resulted from the use of bismuth paste in the treatment of an empyema. The most striking feature of bismuth poisoning is the stomatitis. It is characterized by patches of a brownish-purple color appearing on the tongue, buccal mucous membrane and the throat. In severe cases the teeth become loose, the gums are spongy, and there is more or less salivation. The breath is very foul and there is difficulty in swallowing. In one case I observed there was a marked unilateral parotitis. The lesion usually begins at the level of the molars and is most severe where the teeth come in contact with the mucous membrane. In addition to the action of the drug on the mouth, the viscera are often involved. The kidneys may be congested and show marked parenchymatous changes. The liver often is the seat of cloudy swelling. The small intestine is deeply injected and the deposition of small particles of the bismuth may give the mucosa a steel-gray color. Over Peyer's patches, coarser black granules may be seen.

Most of the cases of poisoning have followed the ingestion of large quantities of the drug for *x*-ray diagnosis of gastro-intestinal conditions. Beck, who introduced bismuth paste in the treatment of empyema and tuberculous fistulae, states that in not a few there is some pigmentation of the gums, thus indicating the absorption of the drug. A few cases have followed the prolonged internal use of the drug. In the case I saw, there was an intense stomatitis, and the urinary findings indicated a severe nephritis.

Bitter Tonics. The action of bitter tonics on the secretion of gastric juice is described by Moorhead,² who studied the reactions of pathological as well as of normal animals to such medication. In Moorhead's study of the action of bitters upon normal dogs, he found that whether these drugs were given by the mouth or sent directly into the stomach they had no appreciable influence upon the appetite nor any material effect upon the gastric secretion, either as to quantity or quality, except possibly a diminution of total acidity. To this extent his studies are in accord with earlier ones of Carlson, who administered bitters to normal men and normal dogs and found that they had no effect which was advantageous, and that sometimes there was a diminution in the quantity and quality of gastric secretions rather than an increase. Quite

¹ Journal of American Medical Association, February 26, 1916.

² Journal of Pharmacology and Experimental Therapeutics, December, 1915.

different results however, from those occurring in normal animals followed when Moorhead administered bitter tonics to dogs which were in poor health because of chronic anemia artificially produced by repeated bleedings. In these cases, a distinctly favorable influence was exerted upon the appetite, although the animal did not consume an amount of food which was equal to the normal because of its feeble condition. He states that there can be no question that the influence of these bitters is definite and significant. When given by the mouth they cause both an increase in the quality and quantity of the gastric juice, the pepsin content remains fairly constant and the change is both in the free and total acidity. Here, again, the amount of gastric juice was not up to the normal, but nevertheless it was above that which was secreted without the influence of these drugs. Another interesting point developed by Moorhead is that these bitters introduced directly into the stomach of cachectic dogs have no appreciable influence upon the quantity or quality of the gastric secretion, which would suggest that the secretion is caused reflexly through the nerves of taste and not by any direct stimulation of the stomach itself.

Blood Serum. Lignières¹ advocates the use of *horse serum in the treatment of wounds*. He has found that serum drawn twenty-four hours after the first blood-letting has a greater curative action than serum from the first. This is probably due to the regenerating process going on after the first bleeding. Compresses are dipped in the serum thus obtained without heating, and are changed once or twice in twenty-four hours. If the serum is to be kept or transported, there should be added to it phenol, not less than 0.5 per cent.

In the treatment of *purpura hemorrhagica*, Emsheimer² relies on the use of blood serum or whole fresh human blood. Blood serum may be injected subcutaneously or intravenously, while whole fresh blood may be given by transfusion or injected intramuscularly. The latter is a simple, harmless, effective procedure, and should be employed before other radical measures in all cases of severe purpura hemorrhagica. In addition, it may prove useful in hemophilia and other blood diseases, in bleeding from various organs of the body, in wasting diseases, and in many infections.

Hurwitz and Lucas³ state that the essential defect of hemophilic blood is a diminution of the circulating prothrombin, which accounts for its delayed coagulability. No definite relationship can be shown to exist between the extent of the prothrombin deficiency and the gravity of the clinical symptoms. Hurwitz and Lucas found that the oral, subcutaneous and intramuscular injection of *kephalin* had no effect on the disease process. If, however, the kephalin is applied locally to the

¹ Bulletin de l'Académie de Médecine, November 9, 1915.

² Journal of American Medical Association, January 1, 1915.

³ Archives of Internal Medicine, April, 1916.

bleeding wounds of hemophilies, the hemorrhage is arrested early. They also recommend kephalin in the treatment of bleeding from external wounds because of its great hemostatic properties and its thermostability.

BLOOD TRANSFUSION. By applying the principles of Moss (1910) in regard to iso-agglutinins and iso-hemolysins, Brem¹ has been able, with certain modifications, to obtain very satisfactory results in transferring blood from one individual to another, and by comparatively simple technic. Moss found that all normal and pathological bloods alike could be classified into four groups by agglutination tests of the serums against the corpuscles. By having donors from each group available, it is possible to furnish blood to any patient, whatever his group may be, after it has once been determined what his grouping is, and thus prevent the group reactions, that is, such reactions as arise as a result of mixing two bloods, the serum of one or both of which agglutinates the red cells of the other. Such reactions are quite typical and come on quickly after the transfusion.

Brem describes the symptoms as follows: There is a feeling of fullness in the head, suffusion of the face and eyes, precordial distress, dyspnea, coughing, backache, rapid and small pulse, which may become imperceptible at the wrist, and sometimes complete loss of consciousness and convulsions. Hemoglobinuria may occur. The shock is very much like the anaphylactoid shock, only in Brem's cases the urticarial rash was absent.

The following plan is adopted for furnishing blood: Numerous donors are separated into their respective groups, and, in addition, Wassermann tests are made. The laboratory keeps in touch with these donors, who are glad to give several hundred cubic centimeters of their blood for a small sum of money. They come to the laboratory, and, by the needle and vacuum flask method, the quantity of blood desired is withdrawn. Some of these donors have been used by Brem many times during four years. They lose no time from work, the procedure is practically painless, they feel that the money is easily earned, and the patient is under no obligation to the donor. The advantage of the method is that the donors are classified, and have negative Wassermann tests which makes it possible to give the transfusion without undue delay.

Boric Acid. The use of boric acid in the treatment of *ivy poisoning* is advised by Lane.² He covers the affected areas with two or three thicknesses of gauze or cheese-cloth, which is kept constantly moist with a solution of boric acid. The strength of the solution is unimportant. The gauze is frequently changed, the guide being the amount of oozing which takes place from the blebs. The larger blebs are opened but the smaller ones are left untouched. If the gauze is used more than

¹ Journal of American Medical Association, 1916, lxxvii, 190.

² Medical Record, September 11, 1915.

once, it is rinsed and boiled before using again. Itching may be relieved by sponging the affected areas with a weak solution of alcohol when the gauze is changed.

A simple ointment, such as zinc oxide, may be employed after healing has begun.

A case of poisoning from the internal use of boric acid is reported by Willson.¹ The case was that of an infant, seven weeks old, to whom about 3 ounces of a saturated solution of boric acid was given instead of boiled water. The child suffered some hours later from severe vomiting and purging. The stools finally consisted of nothing but clear, jelly-like mucus. The vomiting and purging continued for thirty-six hours. Two days after the ingestion of the boric acid a slight miliary eruption appeared on the neck, chest, and back. The baby made a good recovery.

Cannabis Indica Intoxication. Like other drugs affecting the cerebral mental centers, cannabis indica shows wide variations in its effects on the higher centers of different individuals. Two cases typical of this, that occurred quite a number of years ago, are reported by Burr,² one of these being himself, the other a fellow interne, each observing the other, and, as far as possible, himself, and careful notes being immediately recorded. Each took 60 drops, one following the other after a period of four days. Except that both had a palsy of accommodation, dryness of the mouth, thirst, and termination in deep sleep, their symptoms were entirely unlike. In one, there were convulsions without loss of consciousness, in the other, there were repeated attacks in which fear of death from suffocation was a most marked phenomenon, though the breathing was perfectly quiet. In one, there was alteration in time-sense, and a feeling of enlargement of space, and he had an hallucination. All these symptoms were absent in the other. These cases illustrate Burr's point, that drugs which, in large doses, cause unconsciousness and in smaller ones affect the emotional and intellectual side of man, vary in the symptoms they cause in different people before unconsciousness is reached. Other drugs behaving in the same way are alcohol, opium, cocaine, and, in less degree, ether. The mental effect with these drugs may vary greatly, while the physiological action of drugs which affect only organs other than the brain is much more constant. It is impossible to tell what types of individuals are going to act alike in their mental cerebral response to drugs. Superficially nervous people sometimes reacting relatively mildly, and those appearing more stolid at times reacting more violently to the same dose, so that the cerebral action of drugs cannot be employed in making a psychological classification of man, though there is a close relationship between drug action and personality.

¹ Washington Medical Annals, November, 1915.

² Therapeutic Gazette, August, 1916.

Chenopodium. Last year attention was called to the favorable reports on the use of oil of *chenopodium* in the treatment of *uncinariasis*. Bishop and Brosius¹ report on its use in 108 patients, 92 of whom received the chenopodium alone, the remainder being given alternate treatments of thymol and oil of chenopodium. The oil is put up in capsules of 8 minims each. Two capsules are given at each dose. One treatment consists of three such doses given two hours apart. Each treatment is followed in four hours by 2 ounces of castor oil. They purposely omitted chloroform from the castor oil, as recommended by Levy, in order to give the chenopodium a better trial. Their conclusions are as follows:

1. The method of administration of chenopodium is simple, and is attended with less inconvenience and discomfort to the patient than with thymol. This would give the drug an important place in the field of *uncinariasis*.

2. Chenopodium can be given at shorter intervals than can thymol, and a cure can thereby be more quickly established, which gives it a greater economic value.

3. Chenopodium is non-toxic in therapeutic doses.

4. Chenopodium is a more efficient vermifuge than thymol in the treatment of *uncinariasis*.

Chlorine Gas Poisoning. The present war has made it possible to study on a large scale the effects of poisoning with chlorine gas. Hill² states that a typical case on admission is cold, with a subnormal temperature, is conscious but restless, with a pulse slow and full, except in the collapsed cases. The face is cyanosed, intensely so in many cases, and the expression strained and anxious. The posture varies. In some cases the patient sits propped up, with head thrown back, gasping for breath; in others, he lies on his side, with his head over the edge of the stretcher in an attempt to aid expectoration. The respirations are jerky and hurried, often numbering 40 to a minute, and are associated with a choking cough, accompanied by a varying amount of frothy expectoration. With each inspiration the chest is expanded to its fullest, all the auxiliary muscles being brought into play just as in an asthmatic paroxysm. This is the first or asphyxial stage, which, if the patient survives, gradually passes off after some thirty-six hours. After this stage the patient falls into a sleep and awakes feeling much better. But after a few hours of comparative quiet, symptoms of bronchitis begin to be manifest. In the majority of cases, these are said not to be severe. In the cases which are kept alive with difficulty, there is a short quiescent stage followed by intense bronchitis. Frothy expectoration gives place to greenish, mucopurulent expectoration, consciousness to delirium, the temperature rises from subnormal up to 104° F., the pulse volume becomes small and its

¹ Journal of American Medical Association, November 6, 1915.

² British Medical Journal, December 4, 1915.

rate increased to upward of 160, the respirations are less choking but more shallow, and number up to 70 before death.

In the *treatment* of severe cases, an urgent indication is to get rid of the exudation in the air passages which threatens to drown the victim. Artificial respiration and insufflation may, therefore, be useful. Emetics are serviceable, as the vomiting aids in freeing the lungs from fluid. The administration of oxygen relieves the cyanosis and improves the condition of the patient. The same general treatment to support, check, and lessen shock is required in chlorine gas poisoning as in extensive burns of the skin. Pneumonia and bronchitis follow chlorine poisoning just as septic infection is the sequel of cutaneous burns. In severe poisoning, in the experimental animals of Hill, pneumonia and bronchitis seem to be the rule, and no means of preventing them appear available. Warmth and good nursing may pull a man through; but those conditions are hard to apply to animals.

Corpus Luteum. Hirst¹ has employed the extract of corpus luteum in five cases suffering from the *nausea of pregnancy*. In four of the cases it was entirely successful. He based his use of the drug on the presumption that there is more than a coincidence between the formation and disappearance of the corpus luteum of pregnancy and the cessation of nausea. It is not unreasonable to suppose that there is sufficient absorption from the corpus luteum of pregnancy to account for the disappearance of the nausea, especially when one realizes that the nausea begins to diminish at the time the corpus luteum has reached its acme of development.

Hirst administered the drug hypodermically in doses of 1 c.c. of the extract (20 mg.) daily. He believes that this dose is too small and should be materially increased.

Cyanocupral. One number of the *Journal of Experimental Medicine* (August 1, 1916) is devoted to this preparation. Three of the articles deal with *tuberculosis* and one with *leprosy*. All of them are contributed by Japanese observers. Koga summarizes his experimental results as follows: The effect of a single injection upon the lesions is either negative or inconspicuous. But after repeated injections of the preparation, the congestion and leukocytic infiltration about the lesions are markedly decreased, the cheesy material resulting from degeneration of the lesions and other degeneration products are in process of absorption, and young connective tissue is being actively produced in the periphery. While these changes are taking place, the number of bacilli is also being reduced, until finally they can no longer be detected on microscopic examination. Koga believes that the experiments he has reported leave no doubt that the substance is capable of bringing about the healing of experimental

¹ Journal of American Medical Association, February 26, 1916.

tuberculous lesions; but, thus far, that most important problem in chemotherapeutics, namely, the extent of the cure produced, has not been solved. The experiments indicate that sterility of the tissues, as far as microscopic examinations go, has been secured; but microscopic examination is not, after all, an absolute test of sterility.

In a second paper on the clinical use of cyanocupral, Koga gives directions as to its administration. As the preparation is highly irritating to the tissues, neither subcutaneous nor intramuscular injection can be employed. The drug is given intravenously. Based on his experimental work, he believes that 0.6 gm. may be introduced without injury, into the veins of a man weighing 60 kilos. But for curative purposes, the dose seems to be 0.1 gm. Owing to individual differences, he began with 10 mg. doses in human beings.

The preparation is colorless, transparent, and of neutral reaction. If allowed to stand in the air for more than six hours, crystallization sets in. It must be used, therefore, as soon as the ampules are opened. After an injection, the patient must be kept absolutely quiet in bed until reactions disappear. As a rule, three, seven, and fourteen days are the periods during which patients in the first, second, and third stages, respectively, must be kept quiet. Extreme emaciation is a contra-indication to its use.

Otani reports on the clinical use of cyanocupral in 16 cases. The interval between doses should be two weeks. Prolongation of the interval may be made without harmful effects. If, however, the reaction produced by the injection should last more than one week, the succeeding injection must be postponed.

The reaction consist of slight fever lasting for two or three days, rarely more than a week. The fever is sometimes preceded by a chill. The general symptoms consist of headache, pain in the limbs, loss of appetite, etc. As a rule, there is some focal reaction and during this period there is often an increase in the cough and expectoration; occasionally there is some blood in the sputum. In pulmonary cases, the maximum dose is 8.5 c.c., and this should never be exceeded.

Otani believes that cyanocupral is a very effective method of treatment. The shortest interval between injections should be two weeks. If given at shorter intervals, no improvement is noted and the effects are sometimes dangerous. In order to obtain the best results, the patient should be placed under conditions of complete physical and mental rest after the injection; this applies even to light cases. Care should be taken also to secure rest for the lesion.

During the period of treatment, irritants to the lesion, such as potassium iodide or tuberculin, should be avoided; apricot juice, guaiacol and its derivatives, and iodol are contra-indicated. No marked idiosyncrasy was noted, and no accumulative effects were observed.

Takano used cyanocupral in six cases of leprosy with apparently beneficial results.

Diet. Diet in *Chronic Heart Disease* is commented on by Hare in the *Therapeutic Gazette* for May, 1916. The first point made is that many physicians pay insufficient attention to the question of the patient's diet when they are treating them for diseases not necessarily associated with disordered digestion. If for no other reason, attention should be paid to this matter because patients expect it, and, if dietetic advice is not given, they may think that the physician is careless. Hare considers that the institution of a very limited diet, both as to the variety of food and the quantity which is taken, is rarely necessary in cardiac disease so far as the cardiovascular condition is concerned. When digestive disturbances exist, these, of course, demand proper dietetic restrictions. But when the diet is reduced below the amount required for a healthy person at rest, the body turns upon itself and so uses up its own tissues, so that eventually distinct emaciation occurs. In the majority of cases of heart disease, whether they be instances of ruptured compensation due to valvular lesion, or failing circulation due to myocardial degeneration, the chief endeavor of the physician is to put more strength into the heart muscle, and how can an exceedingly low diet be compatible with this effort? It certainly would not be considered compatible with an effort to increase muscular strength in other parts of the body.

Food easy of digestion, frequently administered, or food which is pre-digested and frequently administered, will often produce the best results, since the taking of two or three hearty meals may, by giving the digestive apparatus a difficult task, also require of the circulatory system too great activity. Objection is offered to any general statement to the effect that coffee, tea and chocolate are injurious to those suffering from heart disease. It is considered that the etiological factor in the production of the cardiac lesion has possibly more to do with the regulation of the diet in heart disease than the actual lesion which is present. Thus in gouty persons it is obvious that foods which are notoriously gouty, like concentrated soups, various forms of game, liver, sweetbread, and other substances are to be avoided. In acute rheumatic fever, when the period of convalescence is established, even if the heart has been badly touched, as full diet as the patient can manage, even including red meat, is to be encouraged, because of the profound anemia and feebleness that may follow this as other infectious diseases. Hare seriously questions the common belief that the liquid intake should necessarily be reduced to save the labor of the heart, contending that the fluid may fail to be absorbed, or if absorbed, may readily be secreted by the kidneys or deposited in the tissues till it can be eliminated. Of course, if there are associated conditions interfering with elimination or promoting retention in the tissues it may be necessary to cut down the liquids.

DIET IN RHEUMATOID ARTHRITIS. Discussing the metabolism and treatment of rheumatoid arthritis, Pemberton¹ reaches the following conclusions:

1. The general conclusions already published as to the application of a restricted dietary in rheumatoid arthritis find confirmation within the limits indicated in the present series of 19 cases.

2. In cases rendered free, or nearly so, of acute symptoms by dietary means, exacerbations have been caused as an "experimentum crucis" by the ingestion of pure carbohydrate. Upon the withdrawal of this, the symptoms have again subsided. The conclusion seems unavoidable that carbohydrate is a factor in the etiology and treatment of many cases of this disease.

3. Contemporaneously with natural or induced exacerbations of the disease, there seems to be a tendency for the urine to show a decreased acidity, as measured by the hydrogen-ion concentration.

4. Observations on the carbon dioxide tension of the alveolar air in these cases show no great departure from the normal.

5. The non-protein nitrogen and urea of the circulating blood in uncomplicated cases of rheumatoid arthritis, examined both during ill health and convalescence, fall well within the normal range.

DIET IN GASTRIC DISEASES. Friedenwold² emphasizes the important part diet plays in gastric disorders. "Diet often," he says, "even exceeds the importance of the choice of drugs. Absolute dietetic regulations cannot be formulated in this class of diseases. Individual characteristics in the patient and in his disease, peculiar tastes, the digestive capacity of the stomach, the importance, especially in chronic conditions, of maintaining proper nutrition, are points demanding consideration. The amount of nourishment will depend on the patient's weight, 35 calories being required for each kilo of body weight, when the individual is at rest. It is advised to weigh every patient suffering with a stomach disorder when treatment is first inaugurated, and to repeat this from time to time, in order to determine any gain or loss in weight. Inasmuch as the proteins can be replaced in a measure by the carbohydrates and fats, an interchange of any of these three food elements can be made according to the patient's condition."

In cases of oversecretion, an abundant protein diet is advocated to neutralize hydrochloric acid excess, red meats and eggs being especially recommended, the carbohydrates to be given in the most easily digestible form. "In cases in which there is a diminution of the gastric secretion, the protein foods are digested with difficulty, whereas the carbohydrates are more easily digested. In this condition, therefore, only very tender meats, preferably scraped, are to be given; whereas such easily digestible

¹ American Journal of Medical Sciences, March, 1916.

² Therapeutic Gazette, February, 1916.

vegetables as spinach, mashed potatoes, and farinaceous foods may be given in quite large quantities. In both conditions of increased and diminished secretion of acid, a reasonable amount of fat must be eaten, preferably in the form of good butter. The diet in muscular disturbances of the stomach depends greatly upon whether an excess or a deficiency of gastric juice is secreted." "In both conditions the ingestion of fluids should be reduced as far as possible." It is pointed out that the appetite, when lost, often leads to the taking of insufficient nourishment, and may, therefore, be an incompetent guide. When the patient does take too little nourishment, his requirements can be diminished by quiet rest in bed. The value of thorough mastication, regular intervals between meals, and of the temperature of food, about 98° to 100°, neither too hot nor too cold, and of intestinal alimentation, are discussed. "Even in cases in which the secretion of the stomach is lost entirely, the intestine may assume the function of the stomach." The question of rest or exercise after eating is one of considerable importance to those suffering from gastric disturbances. It is generally admitted that violent exercise should not be indulged in after eating. From my own observations, it appears that in conditions of gastric disturbances accompanied by increased or decreased acidity, and in muscular disturbances of the stomach the gastric digestion is improved during rest, but impaired by sleep after meals.

The value of Bulgarian buttermilk is heartily endorsed on account of its digestibility, due to the fact that the casein and albumin in the milk have been rendered soluble. Olive oil in certain gastric disorders, for example gastric ulcer, is recommended, both as a food and as a remedy.

The author has obtained most gratifying results in a large number of cases of peptic ulcer by a method evolved by Lippey, the treatment consisting in protecting the ulcer from the acid corrosion until it has healed by shielding it from the corrosive effect of the gastric secretion. "He accomplishes this by maintaining a neutralization of all free hydrochloric acid from early in the morning until late at night. This is effected by frequent feedings and the use of alkalies given frequently. The patient remains in bed three or four weeks. Three ounces of a mixture of equal parts of milk and cream are given every hour from 7 A.M. to 7 P.M. After two or three days, soft eggs and well-cooked cereals are gradually added until in ten days the patient receives 3 ounces of milk and cream mixture every hour, 3 soft-boiled eggs, and 9 ounces of a cereal each day. Cream soups of various kinds, vegetable purées, and other soft foods may be substituted now and then as desired. Powders of magnesia and soda, and bismuth and soda are given between the feedings to neutralize the acid secretion."

Duodenal alimentation, devised by Einhorn, that is alimentation by the direct introduction of food into the duodenum, is regarded as being

of the greatest importance. As much as 2280 calories can be administered by this method in twenty-four hours.

Drug therapy, especially atropine, hydrochloric acid, and pepsin, receive comment in this paper. Mineral-water cures and the indications for surgical intervention in gastric disorders are also discussed.

THE FOOD PROBLEM IN DISPENSARY PATIENTS OF DIFFERENT NATIONALITIES is the subject of a paper presented by Landis and Craig at the meeting of the Association of American Physicians in May, 1916. The proper utilization of food has an important bearing on the prevention of disease, notably tuberculosis. Are the people getting the right kind and amount of food for their money? Are foreign-born dispensary patients adapting themselves well to American market conditions? A study was made of four groups of families: three Italian, three Jewish, three Negro and three Polish. Daily inventories of their food supply were made for three weeks by a nurse; calories, waste, and cost were estimated. Adopting a standard calory value, including 340 calories represented by protein, it was found that all the groups approximated the desired calory value in the food purchased, but there was much variation in the protein content. The cost per head per day was as follows: Italian, 19 cents; Jews, 21.5 cents; Negroes, 24 cents; Poles, 34 cents.

While it would be unwise to lay too much stress on any one cause as responsible for disease of the teeth, the RELATION BETWEEN DIET AND DENTAL DISEASE has certainly been established as a most important one, and one to be always considered in the prophylaxis and treatment of such diseased conditions. In this connection, an article entitled "The Influence of Diet on the Development and Health of the Teeth" by Durand¹ is of special interest.

"During the past year I have enlarged these statistics by an examination of children at the Better Babies' Contests, held in Seattle and Bremerton, Washington, and children seen in private and dispensary practice. My results seem to confirm the earlier statistics."

From better babies contests Durand obtained the following results:

Food.	No. examined.	No. showing caries.	Percentage of caries.
Breast milk	418	118	28.2
Cows' milk mixtures	102	30	29.4
Sweetened condensed milk	32	17	53.1

Of 104 cases collected from private and dispensary practice in which the children had been fed five months or longer on sweetened condensed milk, 77, or 74 per cent., showed caries of the teeth.

He points out that the significance of these statistics is that a poorly balanced diet, high in carbohydrate and low in fat, protein, and mineral

¹ Journal of American Medical Association, 1916, lxvii, 564.

constituents, fed during the period in which the teeth were developing and calcifying in the jaws, seems to have rendered them doubly susceptible to decay after they erupted.

These facts emphasize the importance of a well-balanced diet during infancy. Such a diet he considers should consist of breast milk, or a properly modified cows' milk when this is unobtainable, with the early addition of vegetables, fruits, and meat. Alfred Hess says that orange juice may be begun any time after the first month. Vegetables, fruits, and meats, properly prepared and given in small but increasing amounts, may be safely begun as early as the sixth or seventh month.

Secondly, he urges giving early a diet which will teach the proper function of the jaws and teeth. A child raised on pap will not learn to chew its food. But if given strips of tough meat to chew the juice out of, such foods as bacon rinds, bones, tough crusts, hard breads, and, later, apples, celery, lettuce, etc., the muscles of mastication and in turn the jaws are enlarged and strengthened. More room for developing teeth is given, and they are hardened, cleaned, and polished after they erupt.

Finally, he emphasizes the importance of preventing decay, which may be effected through selection of food and its proper sequence during a meal. The last article eaten should be one which will cleanse the teeth and leave no sticky carbohydrate, decay-producing residue. A tooth-brush will not remove sticky pastries, cake, and other carbohydrate remains from the fissures of the teeth, but meat, a green salad, celery, radish, onions, apple, oranges and fibrous food generally, under the 100 to 250 pounds' pressure of the healthy bite, will grind such food out and the residue left, if any, will have a detergent action toward caries. Pickerill, in his exhaustive work, has shown that the amount, ptyaline-content and alkalinity of the saliva secreted in response to various flavors, acidity, and hardness of foods varies greatly. Acid fruits produce much highly alkaline saliva, a high ptyaline content, and are an ideal food with which to finish a meal.

THE PASTEURIZATION OF MILK. With all its drawbacks, for example, the injury to the milk, and the possibility of carelessness in the manipulation of milk sold as pasteurized, thereby placing the purchaser in a position of false security, in spite of its disadvantages, pasteurized milk as a commercial product demands consideration. The importance of this procedure is urged in an editorial article.¹

Pasteurization is today the most available process for the destruction of bacteria in milk on a commercial scale. As practised at the present time, heating to 145° F., and holding at that temperature for thirty minutes, followed by rapid cooling. With reasonable care, pasteurization destroys about 99 per cent. of the bacteria; and while it does not

¹ Journal of American Medical Association, 1916, lxxvii, 683.

prevent the ultimate souring of the milk, it does delay the process. The editorial points out the need of national education as to the merits and advantages of pasteurization, especially in the smaller communities where the method is but little used. In the large cities, pasteurization is becoming more and more the method of choice.

Goodman¹ has employed the KARELL DIET in cases of renal, cardiac and hepatic edema with good results. His best results were obtained in those cases which are best termed myodegeneratio cordis, the type of cardiac disease seen in senility, emphysema, chronic alcoholism, and in cachectic states. In this type, the results were favorable in 60 per cent. of the cases treated.

Under the combination of rest in bed and the Karell diet, the pulse assumes first, a better quality, and later becomes less irregular and less frequent. Blood-pressure is lowered, particularly in cases of renal hypertension. He found that diuretics and cardiac stimulants, such as digitalis, theocin, camphor, strophanthin, and caffeine, often failed to give favorable results when used alone; when, however, they were used in conjunction with the Karell diet, they acted especially well.

ALLEN TREATMENT OF DIABETES. Commenting editorially on the Allen treatment of diabetes, the *Therapeutic Gazette* (June, 1916) advises caution in the use of this mode of treatment. It is considered a good rule and practice "to recognize the fact that no one routine method of treatment can be employed in all patients suffering from the same disease, since that which suits one patient may be quite improper or ill-advised for another. In other words, the recommendation that the Allen treatment be instituted promptly in every case is, we believe, unfortunate and unwise. For these reasons we have perused with much interest a contribution by Joslin, Brigham, and Horner, in the *Boston Medical and Surgical Journal* of March 16 and 23, in which they report 14 cases of diabetes mellitus unsuccessfully treated by fasting. Possibly no one in this country has done more toward the scientific investigation of this obscure malady than Joslin, and therefore anything he may say in regard to this matter is of the greatest possible importance."

It is only fair to state that, in the opening of their article, these writers say that they thoroughly believe in the fasting treatment of diabetes as outlined by Dr. Allen, and that under this treatment their diabetic patients do better than ever before. They go on to say, however, that their object in publishing this paper is to show that some of the patients so treated have died, and to point out the apparent failure. They have used alkalies less and less in the treatment of acid intoxication, endeavoring to avoid the necessity for the use of alkalies by preventing acidosis. They have found it advantageous, however, in long-standing and complicated cases, without otherwise changing the habit or diet, to begin the

¹ Archives of Internal Medicine, 1916, xvii, 809.

treatment of omitting the fats in order to decrease the source of the acid bodies, after two days to omit the protein and simultaneously to halve the carbohydrates daily to 10 grammes, and then, if sugar has not disappeared from the urine, to fast the patient.

The opening paragraph of the second section of their paper states in different words, the views we have already expressed in this article as follows:

"Changes in the diet and regimen of patients who have suffered from diabetes for many years are always dangerous, and particularly so when the case is of extraordinary length. Treatment of such individuals should never be undertaken lightly nor without a full realization of the gravity involved." These authors close their paper with these words:

"The experience derived from these patients has led us to adopt a preparatory treatment to fasting for very severe, long standing, and complicated cases."

The editorial concludes by stating that the point which the writer wishes to make, and emphasize, is not that the Allen treatment of fasting diabetics is essentially erroneous, or that it will not, in a large number of cases, produce excellent results, but that it cannot be applied haphazard in all cases, and that, if so applied, it will sometimes induce disaster, for every case of diabetes should be approached by the physician "reverently, discreetly, and in the fear of God!"

Digitalis. From his electrocardiographic studies of patients under digitalis treatment, Stevens¹ reaches the following conclusions:

1. The cases in which digitalis produces marked slowing of the heart are cases of abnormally rapid rate; the drug in ordinary doses appears to have little or no effect upon rates which are normal. The ventricular slowing may be produced in cases of normal auriculoventricular sequence and in cases of auricular fibrillation and auricular flutter.

2. In some cases of normal rhythm under digitalis treatment, there is a distinct increase in the P. R. interval, and an accompanying increase in the R. T. interval. In some cases of fibrillation, also, the increase in the R. T. interval is found. In most instances these increases are coincident with a decrease in the rate, and hence accompany an increase in the length of the whole heart cycle. A possible factor in the improvement of the heart's action under digitalis may be the increased mechanical advantages resulting from the increase in the total length of the cardiac systole.

3. Transformations in both P. and T. waves appear coincidentally with and are apparently related to, the digitalis treatment. These variations are, however, not constant.

4. A single case in which digitalis coupling occurred shows, in all

¹ Boston Medical and Surgical Journal, March 9, 1916.

instances of the extrasystolic, complexes of the same type, indicating a common focus of origin.

5. A single patient showed a much increased susceptibility to slowing by vagus pressure during the digitalis treatment.

CLINICAL STUDY OF VARIOUS DIGITALIS DRUGS. The relative value of the various drugs making up the A. digitalis group from the clinical stand-point differ from each other mainly in the rate and certainty with which they are absorbed and excreted, and in their local action before absorption. Such has been the experience of Halsey,¹ who says that clinically there appear to be no qualitative differences of practical significance in their all-important actions on the circulation.

As to the digitalis preparations, he prefers the tincture. Any preparation which is advertised to be free from cumulative action is, in his opinion, worthless, as to be of value the ability to cause such an action must be present. If it is removed, the drug is of no service. He favors strongly digipuratum because the active principles are present in a form in which they are insoluble in the stomach, consequently they do not irritate the gastric mucosa. Furthermore, it is a preparation of very uniform strength. Its high cost is the only objection to making it the method of choice for oral administration. Digitalin he believes to be too uncertain in its composition and strength. He has found some samples to be twice as powerful as others.

The effects of digitalis on *auricular fibrillation* are considered in the *Therapeutic Gazette* (April, 1916), which deals largely with a paper by Cattle. It is pointed out that while digitalis is useful for the purpose of toning up the cardiac muscle in dilatation and many forms of cardiac weakness, it is in cases of fibrillation that results are often achieved which exceed in brilliance those due to the use of the drug in any other circumstances. Doubtless the tonic action of digitalis on the muscle and on the vagus nerve partly accounts for this favorable result, but, considering that the effect is so much greater in fibrillation than in other forms of irregularity, it seems most probable that the more regular and more forcible contractions of the ventricles are due also to the "blocking" action of digitalis, by means of which some of the abnormal impulses from the fibrillating auricles are cut off. In using a powerful drug like digitalis, it is necessary to have a clear conception of the conditions it is likely to benefit. There could be no greater mistake than to give it indiscriminately to every patient who had a murmur. It should not be given for premature systole, as the disturbance is one digitalis is very liable to produce. It is recommended to give the drug cautiously in heart-block, but freely if the block is complete.

The dose of tincture of digitalis advised for cases of fibrillation is fifteen minims four times a day. In case of urgency the dose may be

¹ Southern Medical Journal, August, 1916.

increased or supplemented by the injection of 5-minim doses of Hoffmann's digalin. The pulse generally drops from 100 to 60 within a week. This is a signal of withdrawing the drug for a few days, to be resumed as the pulse-rate increases, and continued at such doses as will maintain the pulse-rate at about 70. Signs of digitalis sufficiently will call for its suspension or reduction are: slow pulse, vomiting, loss of appetite, diarrhea, scanty urine, and coupled beats, the last mentioned danger sign having been emphasized by Mackenzie and Lewis.

In considering the value of digitalis in *aortic insufficiency*, Taylor¹ expresses his disbelief in the value of the drug for this condition, and records a number of cases having aortic regurgitation who have survived to old age to whom digitalis has never been given since he has had them under observation, now some ten to fifteen years.

In the treatment of the *arrhythmias*, Christian² states that in some cases with auricular fibrillation in which edema is marked, a much better diuresis is obtained by combining with the digitalis a diuretic drug, such as theocin. In cases with auricular flutter, digitalis usually produces a striking effect. In paroxysmal tachycardia there is little evidence that digitalis produces any good effect.

In considering the treatment of *high blood-pressure*, Elliott³ states that digitalis is the most useful drug we possess no matter what the origin of the trouble is. The fact that the blood-pressure is high need not deter us from using digitalis. It acts just as well, and even better, with a high pressure than with a falling pressure. Indeed, he asserts it will lower a rising pressure and raise a falling pressure, providing cardiac embarrassment is the underlying cause. He urges the use of digitalis at the very first appearance of cardiac decompensation believing it to be a great mistake to reserve its use until cardiac failure is established. This is because we are dealing with an exhausted degenerated heart muscle which should be aided before it is placed at too great a disadvantage.

Emetine. Discussing the avoidance of *toxic manifestations* from the use of emetine, Levy and Rowntree⁴ from clinical and laboratory observations have the following suggestions to offer:

1. The administration of emetine hydrochloride is not to be regarded as a harmless procedure. Even in therapeutic doses ill effects may follow its use.

2. Individualization by close clinical observations is essential both for the success and safety of the treatment. Patients may differ markedly in their susceptibility to the drug, and the various commercial

¹ London Lancet, July 15, 1916.

² Boston Medical and Surgical Journal, August 26, 1915.

³ Journal of American Medical Association, September 18, 1915.

⁴ Archives of Internal Medicine, March 15, 1916.

preparations vary widely in toxicity. These points are strikingly demonstrated by the toxicity experiments reported by the writers.

3. The treatment should be given in courses, at intervals of several days or a week. The subcutaneous route is the one of choice. Individual dosage and the duration of each course must be determined by the exigencies of the case. One-third grain three times a day for a week or ten days is usually a safe dosage in amebic infections. It is rarely necessary to give more than $1\frac{1}{2}$ grains daily. In the treatment of pyorrhea, Bass and Johns advocate one-half grain daily for from three to six days, and maintain that no case need have more than six days' treatment.

Under ordinary circumstances this seems well within the margin of safety. It must be borne in mind, however, that the administration of even relatively small doses over a long period of time may prove harmful.

4. The large dosage advocated by Baermann and Heinemann is unnecessary and dangerous.

5. Intravenous injections should be employed only in extreme cases. If this mode of administration seems imperative, small doses, well diluted (one-half grain in 100 c.c. salt solution), should be slowly given and the blood-pressure should be carefully observed during the injection.

The use of emetine in various *conditions associated with hemorrhage* has received considerable attention in the past few years and good reports about it have come from many sources. Allen¹ has had an opportunity of noting the effects in the case of soldiers who have returned from the front with dysenteric symptoms, accompanied by blood and mucus in the stools. The effect of a hypodermic injection of emetine hydrochloride (one-third grain) once daily has been wonderful; it has been followed by the speedy disappearance of the blood from the stools, while the diarrheic symptoms have likewise quickly improved. In another case of a soldier in training who developed most troublesome mucous colitis, which resisted the usual remedies, the injection of emetine hydrochloride in the dose above mentioned was successful in curing the condition. Allen advocates a more extensive employment of the drug.

Chronic poisoning by emetine has been studied by Dale.² His investigation, still only in the initial stage, was carried on with a small number of cats and rabbits. In all the experiments conducted as long as a fortnight, symptoms of intoxication have sooner or later developed, have become rapidly intensified with persistence in the daily injections, and have terminated fatally. In rabbits, a profuse diarrhea, attended with rapid emaciation, has been the most prominent effect. In cats this symptom has been seen, but is apparently of secondary importance, and may be absent altogether; the most prominent effect in this species

¹ Prescriber, May, 1916.

² British Medical Journal, December 18, 1915.

is pronounced lethargy and somnolence, deepening to a terminal coma. The pathological examination of the material has been begun, and it can only be mentioned, with all reserve, that there is evidence of damage to the liver and kidneys, in addition to the expected signs of intestinal irritation. The doses, though rather large, produced, when given only once, no appreciable effects on the animals. But making all allowance for differences in dosage and conditions in animals and human beings, Dale believes that his results have their significance in indicating a serious danger in pushing the administration of emetine beyond a certain point. His object is not to suggest any modification in the accepted dosage and rate of administration, but rather to re-enforce with the aid of direct evidence the warning, which has already been sounded from other quarters, against the indiscriminate and unguarded use of emetine beyond the limits which expert observation has laid down for its employment with safety and benefit.

The effect of the administration of *emetine during pregnancy and menstruation* is discussed by Chalmers and Papatheodorou¹ in reporting their clinical experience with amebic dysentery. They consider that a half grain (0.03 gram) daily dose of emetine is the maximum which can be given safely in pregnancy. Even the effect of these doses should be carefully watched, and no more of the drug injected than is required to kill amebæ in the stools, all question of a complete cure being set aside until after delivery. It appears advisable to the authors, likewise, not to administer emetine during the menstrual period, though if it is urgently required, it can be given without serious harm and continued in the intermenstrual period. A case is recorded by the authors in which a period suddenly ceased on the second day, apparently the result of the daily administration of half-grain doses of emetine.

Emetine in the Treatment of Amebic Dysentery. The importance of specific treatment with emetine in dysentery caused by the entameba histolytica has been borne out by Low's² experience. He has usually used the hydrochloride and has generally employed subcutaneous injections, 1 grain at an injection being his ordinary dosage. Two such injections are given a day, morning and night, for the first two or three days if the case is a bad one with much blood, mucus, and pain; or, if not, only once a day. After that 1-grain injections are administered every night until a total of 12 grains in all have been given. By this time all blood and mucus should have disappeared from the stool, and amebæ should no longer occur. Not uncommonly, about the fifth or sixth day of treatment, a moderate degree of looseness of the bowels, or in some instances a definite diarrhetic condition, is met with. This may be due to the emetine itself. After the cessation of the drug, the

¹ Journal of Tropical Medicine and Hygiene, quoted by New York Medical Journal December 4, 1915.

² British Medical Journal, November 13, 1915.

stools become solid, of a normal consistence, and no blood or mucus is seen on their surface. They should be carefully searched for amebae, and if these return or if the mucus and blood appear again a second course of emetine will be required. This does not, as a rule, need to be so prolonged as the first, and may be given in 1-grain doses every night until 6 grains in all have been taken. Third courses are practically never necessary. In Low's experience, larger doses than those mentioned are not required. If all symptoms of dysentery have not disappeared by the time the 12 grains are taken, then the diagnosis is in all probability at fault, and the condition is due to some other condition than the entameba. With such doses toxic symptoms do not occur, but it is quite possible that, if the drug is given in larger individual doses and kept up over long periods of time, such might appear. As has been pointed out, there is no need for this, excessive doses not being required. The action of the drug on the vegetative or living stage of the ameba is very rapid, the parasites quickly disappearing, as do also the blood and mucus and other symptoms. Practically all cases of amebic dysentery yield quickly to emetine treatment, there being only a small residuum of definitely diagnosed cases that fail to respond. Such failures still lack explanation. Besides the employment of emetine many other important subjects connected with the treatment of amebic dysentery are discussed in this paper.

Ergot. A case of *tetany* in an adult following *poisoning from ergot* is reported by Emsheimer,¹ certainly a most unusual source for the occurrence of tetany. Gastric and intestinal disorders, particularly dilatation of the stomach, are relatively common causes of tetany in adults in this country. It occurs less frequently in the course of one of the acute infectious diseases, such as typhoid fever or influenza; during pregnancy, after parathyroidectomy, following poisoning from chloroform and various metals, and as a complication of certain organic nervous disease, such as syringomyelia and cerebellar neoplasm.

In this patient, the most striking appearances consisted in the position of her extremities. There was a more or less general rigidity of both arms and legs, and a typical bilateral carpotarsal spasm. The elbows and wrists were acutely flexed, and the hands drawn toward the ulnar side; the thumbs were adducted beneath the fingers; there was flexion of the metacarpophalangeal joints, extension of the phalangeal articulations. The feet were extended at the ankles, the toes flexed at the metacarpophalangeal joints. On questioning the patient as to the cause of her illness, Emsheimer elicited the fact that one week before the onset of the present attack the patient having passed her menstrual period three days, took a large dose of fluidextract of ergot (quantity unknown, as she had taken a swallow of the liquid directly from the bottle), and

¹ New York Medical Journal, December 18, 1915.

continued its use in teaspoonful doses every two hours for five days. She had had some nausea and diarrhea, but no other symptoms of ergotism, up to the onset of the present condition. There was still amenorrhea. Despite the fact that the symptoms of tetany became manifest only after a period of two days from the date at which the ergot was discontinued, there seemed to be no other peculiar phenomenon. The tetany of pregnancy was considered to be ruled out by the fact that tetany occurs in this condition only during the later months. Unfortunately, Emsheimer was not able to make further observations in this case as he did not see the patient a second time. He was informed, however, about one month later, that she had had a recurrence of her acute attack. (This would certainly lay open to question the etiological factor of the tetany in this case.)

Exercise. *The effect of exercise on certain parts of the body*, as for instance the skeletal muscles and the heart, is well understood. As the result of exercise these muscles hypertrophy and this increase in size and strength is susceptible to measurement. What effect exercise has on certain of the vital organs, as for instance, the liver, lungs, kidneys, etc., has never been clear. Some very interesting and important experimental work has been done on this subject by Hatai.¹ His observations were made on albino rats. Determinations were made of various external measurements, visceral organs, ductless glands, etc., in comparable animals. Some of these animals had been allowed to exercise vigorously in revolving cages while the controls led the ordinary lives of rats confined in cages. As the result of long-continued exercise (equivalent in man to a period of from seven to fourteen years) many striking alterations occur in the various organs. The heart, kidneys and liver showed the average excess of about 20 per cent. in size, while the spleen showed a similar amount of deficiency. The brain weight showed an average increase of 4 per cent. but no change was noted in the spinal cord. The ovaries were increased 84 per cent. and the testes 12 per cent. The changes in the hypophysis and suprarenal glands were variable. The heart was increased in size in proportion to the amount of work.

The effect on metabolism of walking and running has been studied by Benedict and Murschhauser.² Benedict, in a previous communication, has shown that very few persons go through a day of ordinary life without having walked a distance of from one to two miles. In a study of the movements of an individual who might be classed as an ordinary office worker, it has been shown that the average distance walked per day amounted to seven miles. Studying the effect of walking and running on the consumption of energy, Benedict and Murschhauser found that when the arms are swung vigorously, as often happens if the

¹ Anatomical Record, 1915, ix, 647.

² Carnegie Institution, Publication 231, 1915.

walking is fast, the metabolism may be increased more than 125 per cent. The amount of energy expended by an average-sized man merely to raise the body at each step amounts to as much as one-fifth. Increasing the speed in walking or running, correspondingly increases the amount of energy expended. One of the outcomes of this study is the practical bearing it has for athletes and workmen as showing the necessity of acquiring a gait or method of performing a manual task which reduces the expenditure of energy to a minimum.

In a study of the *effect of exertion on the circulation* Macphail¹ states that there is a rise in systolic pulse-pressure, although a general vasodilatation may nullify this effect. The diastolic pressure is always lowered, and in failing compensation the fall in diastolic pressure is most pronounced. There is often an almost complete absence of the prediastolic wave pointing to diminished systolic pulse pressure.

There are in use not a few methods of treatment the propriety of which is questionable, but which, by reason of long usage, are persisted in. Thus we continue to follow a plan the rationale of which we do not understand. Typhoid fever, for instance, was long treated by a milk diet, and the danger of employing any other method became so firmly fixed in the minds of the profession that it is only after years of preaching, by a few, that a more rational view has come to prevail. The treatment of *hemoptysis* is subject to this criticism. From time immemorial the belief has prevailed that exercise or exertion tended to produce pulmonary bleeding in phthisical subjects and that the *sine qua non* of treatment was absolute rest. For this reason it is not uncommon to see a patient who has had a pulmonary hemorrhage lying for hours or even days in a fixed position and covered with bedding which has become spattered with blood. The fear of bringing on another attack if the patient moves or if the bedding is changed is responsible for this.

Because of this unnecessary dread, a recent article by Bang² is welcome. He states that the traditional idea that after a hemorrhage from the lungs the patient must be kept absolutely still is based on theory and not sustained by actual facts. In a careful study of the subject of hemoptysis, he found that the initial hemorrhage came on while the patients were lying in bed or reclining in a chair, in 69 per cent. of 354 cases; in 15 per cent. of those while dressing, sitting up in bed or just lying down; in 6 per cent. of those who were walking or working, and in 8 per cent. of those otherwise out of bed. In only 2 per cent. did a hemorrhage occur when the patient was climbing stairs, and yet out of 2000 studied they must have climbed the stairs over 1,000,000 times, taken at least 10,000 warm baths and 25,000 douches while in

¹ British Medical Journal, October 30, 1915.

² Ugeskrift for Laeger, March 23, 1916; Journal of American Medical Association, May 13, 1916.

the sanatorium. No one part of the twenty-four hours seems to be more liable to it than others, and in his cases there were only 10 cases in which the hemoptysis came on while at stool, including 3 primary and 7 secondary hemorrhages. Bang regards it as significant that the condition was constantly febrile in 50 cases; that fever had developed just before the hemorrhage in 45; that it occurred just afterward in 31; 11 had been severely chilled and 10 had been given a tuberculin injection just before. Thus, in 45 per cent. of the cases there were present conditions predisposing to congestion or stasis.

Bang advocates a more liberal method of treatment than that which prevails, by allowing the patient to sit up and move after an hemoptysis. He believes that allowing the patient to sit up, or at least assume a half-reclining posture, has a beneficial effect both on the mind and the appetite. The patient should be allowed to assume one of these postures at once. Rising in bed to a sitting posture presses on the vena cava, as in straining at stool, and is apt to start reflex action from the nerve. He states that this one movement of sitting up in bed is probably what has given movements of any kind such a reputation for being dangerous. This danger, he says, is entirely averted if the patient is placed from the start in a sitting posture. The comfort of the patient is greatly increased as expectoration, eating, and vomiting, the performance of the toilet, etc., and all more easily carried on if this posture is allowed. He makes no change in the diet.

Bang's real object in advocating this plan is that it aids in warding off the evil consequences of extravasated blood. The extravasated blood may sweep tubercle bacilli, pus and mucus from the diseased into sound areas and for this reason natural and voluntary aspiration of this material is important. Allowing of the postures he recommends aids in this act. Although admitting that a certain amount of danger cannot be absolutely denied, Bang believes that the danger looms up larger in theory than in actual experience. Personally, I am inclined to believe Bang is correct in his views, and of recent years I have been inclined to disregard blood-streaked sputum and very small hemoptyses.

Webb, Forster, and Houch¹ advise that tuberculous patients be trained to rest at night and during the day on the more affected side. As a further means of keeping the diseased lung quiet, a small, firm pillow may be placed at the side in order to restrict motion. They state that under this plan there has been a reduction in the amount of sputum and that healing has been promoted, relapses hindered and fever diminished.

Fuchsin. The use of the aniline dyes in the local treatment of ulcers and skin disorders has been referred to in previous issues of *PROGRESSIVE MEDICINE*. Ferreira² reports favorably on the use of fuchsin in the

¹ Colorado Medicine, May, 1916.

² Archives de médecine des enfants, August, 1915.

treatment of *impetigo*, *intertrigo*, and other obstinate skin affections in infants. He employs the ordinary Ziehl's carbol-fuchsin used in bacteriological work. One part of fuchsin is dissolved in 10 parts of alcohol, with 5 parts of phenol and 100 parts of distilled water. This solution is applied by means of cotton to the crusts, pressing the fuchsin mixture into each after all loose and friable parts have been removed with sponges dipped into a 1 to 1200 solution of zinc sulphate or its equivalent. The crusts absorb the fuchsin mixture and harden, forming an impermeable red varnish. The treatment is applied daily. The only objection to it is that it may stain the clothing.

Another of the aniline dyes, *Scharlach R.*, has been studied experimentally by Bullock and Rohdenburg.¹ This is one of the substances recommended for the treatment of *sluggish ulcers*. It is supposed to stimulate the epithelial cells. It is the belief of Bullock and Rohdenburg, however, that *Scharlach R.* exerts no specific stimulating action on epithelial cells.

A remarkable case of *aniline poisoning* is reported by Hartogh.² A young man in robust health was about to take part in an athletic contest, but before it began he became extremely cyanotic, his lips, hands, and nails were blue, as was also his skin. He suffered from headache and vomited. The pulse was accelerated, the respirations quickened, and he was slightly delirious. Hartogh suspected aniline poisoning, and examined the young man's shoes. They were new and had been white, but he had colored them black. He had only been wearing them about an hour and a half. The symptoms quickly disappeared under the use of stimulants, cold water to the head and exposure to the fresh air.

Heliotherapy. In the treatment of *wounds*, Grangé³ has been impressed with the more rapid healing in those cases which have been exposed to the direct sunlight. The scars are less adherent, more supple, and are never harmful. The scar tissue develops normally and does not become exuberant. The deodorizing effect of exposure to the sunlight is direct and immediate. Suppuration is increased at first, as a rule, but later it grows less. He found that patients with severe wounds developed fever and inflammation when exposed to sunlight early. He, therefore, advises a period for recuperation before commencing the heliotherapy. After a period of two or three weeks or a month, even the most destructive wounds showed benefit from the exposures. If there was fever at the time, the temperature dropped to normal.

Grangé exposed the whole of the wounded area, and increased the time of the treatments from half an hour to three or four hours daily.

¹ Journal of Medical Research, September, 1915.

² Abstract, Journal of American Medical Association, September 4, 1915.

³ Paris Médical, December 25, 1915.

Deutschländer¹ placed the wounded in an abandoned greenhouse. He states that severe wounds healed unusually quickly under the heliotherapy thus rendered possible.

Jeanneret² states that even in a city environment, heliotherapy can be made to yield good results. He states that with time and patience tuberculous bone lesions can be cured without going to the mountains. His work was done at the Children's Hospital at Basel. Jeanneret insists that the method is not limited in its usefulness to tuberculous lesions, but that it is the tonic *par excellence* for all debilitated conditions in children. The exposures are commenced gradually, two for five minutes the first day, increasing to two for sixty minutes by the seventh day, and two for three hours by the twelfth day. During the winter months, February for example, the exposures are six or seven times as long as in July, when the sunlight is intense.

Tarole³ has utilized heliotherapy in the treatment of *skin diseases*. Pus-forming affections invariably were benefited by this method. Graded exposures promote general bodily vigor, discourage the growth of bacteria, diminish inflammation, encourage resorption of pathological exudates and of scar tissue, stimulate epidermization, cellular multiplication and reconstruction, and, above all, tend to relieve pain.

Jesionek⁴ treats *lupus* by means of exposure to the direct sunlight or to the rays of a mercury quartz lamp. He advises exposure of the entire body as he believes that the pigment generated in the epidermis by the rays is absorbed into the circulation to a certain extent and carried to the tuberculous focus where it exerts its therapeutic effect. As lupus foci shielded against the light healed under general heliotherapy, Jesionek believes that the general, rather than the local, exposure is the essential factor.

Leukocytic Extract. The therapeutic effects of leukocytic extract have been studied by Schottstaedt.⁵ In a paper read before the American Association of Immunologists, he stated that the work had been carried on with leukocytic extract prepared from leukocytes obtained from the blood of normal animals. Injected subcutaneously into normal individuals and into those suffering from an acute infectious disease, it produced a marked leukocytosis. The leukocyte increase is often 300 per cent., and is highest ten or twelve hours after the administration of the extract.

The neutrophile elements are particularly increased, and, coincident with this, there is a less well-marked increase in the eosinophile cells.

Schottstaedt states that striking beneficial results were obtained in

¹ Deutsch. med. Wchnschr., October 14, 1915.

² Revue Médicale d. l. Suisse Romande, August, 1915.

³ Cleveland Medical Journal, October, 1915.

⁴ Ztschr. f. Tuberculose, December, 1915.

⁵ Journal of American Medical Association, 1916, lxvii, 69.

certain of the acute infections, as furunculosis, pneumonia, acute bronchitis, and acute tonsillitis. Less striking results were obtained in chronic infections.

Hexamethylenamine. Haskins¹ undertook, under the auspices of the Committee on Therapeutic Research of the Council on Pharmacy and Chemistry, a study of the effect of hexamethylenamine on uric acid. It is admitted that perhaps after the administration of excessive doses of the drug, certain portions of the secreted urine may contain a sufficient concentration of it to impart to them a uric acid solvent power greater than the same urines would otherwise manifest. But, as Haskins points out, this is scarcely of therapeutic value. The doses of the drug is too large, and an equal or better effect can be produced more readily by the administration of alkaline diuretics of sodium bicarbonate in reasonable quantities.

Corica² reports on the effects of hexamethylenamine in healthy children and in those suffering from nephritis. In 11 healthy children the drug was found in the urine in half an hour, and the elimination kept up for from twenty to thirty-three hours. In five children with nephritis, the drug appeared in the urine in half an hour also, but the elimination kept up for from forty-six to eighty-five hours. Corica believes that the drug is eliminated through the glomeruli and that its action on the kidneys depends on the nature of the kidney disease. If it is of toxic origin, the drug has less effect, its action being practically restricted to warding off, if possible, ascending invasion of bacteria from the bladder. Invasion of this kind is favored by the scanty production of urine in the toxic cases. In cases of infectious nephritis, the drug has an antiseptic action. In addition, it changes the urine from an alkaline to an acid reaction and aids in preventing the development of bacteria in the urinary tract below the kidney.

In an article dealing with some observations on the elimination of *hexamethylenetetramine*, Falk and Suguria³ state that, in general terms, the amount normally excreted is greater the lower the specific gravity of the urine. The concentration of formaldehyde in the urine had no apparent connection with the amount of the drug excreted. Finally, in a number of pathological cases involving impairment of kidney function, abnormally small amounts of hexamethylenetetramine were excreted.

Hypophosphites. For years the hypophosphites were widely used in the treatment of *pulmonary tuberculosis*. It is difficult to understand their popularity. It is interesting to note that Marriott⁴ condemns them *in toto*. He emphatically states that there is no reliable evidence,

¹ Archives of Internal Medicine, December, 1915.

² Pediatrics, July, 1915.

³ Journal of Pharmacology and Experimental Therapeutics, January, 1916.

⁴ Journal of American Medical Association, February 12, 1916.

either clinically or experimentally, that they exert a physiological effect; it has not been demonstrated that they influence any pathological process; they are not "foods." "If they are of any use, that use has never been discovered." An editorial article¹ is equally emphatic in condemning glycerophosphates. As it pertinently remarks, glycerophosphates will continue to be manufactured until physicians refuse to prescribe them!

Kaolin. Last year attention was called to an article by Hektoen and Rappaport on the use of kaolin in "diphtheria carriers." During the past year Rappaport² has contributed a second article on the subject. Rappaport states that crude kaolin thoroughly dried and sieved may be applied directly to the nasal mucous membrane by means of a powder blower. In children, he carries this out at two-hour intervals for six treatments. Before each application the nose is sprayed with a cleansing solution of sodium bicarbonate and sodium baborate, 2 per cent. each. In adults, the application to the pharynx may be made by having the patient swallow, at two-hour intervals, four half-teaspoonfuls of kaolin. The action of the kaolin is purely mechanical. The bacteria cling to the kaolin, and with its removal the germs are also removed.

Under this method the average stay in the hospital of 100 patients was 25.61 days, while the time of quarantine for a similar number not treated with kaolin was 33.45 days.

A somewhat drastic measure for treating "diphtheria carriers" is recommended by Ruh, Miller, and Perkins.³ They conclude that the condition is most effectively remedied by means of tonsillectomy and adenoidectomy. By this procedure the condition was relieved in a little over eight days, on the average, after the performance of the operation.

Hess⁴ reports favorably on the use of *fuller's earth* in the treatment of *intestinal disorders in infants*. An ounce of the earth may be given in a day's feeding. Mixed with the food (milk) it is taken without difficulty and produces no disorder. In normal infants its sole effect, which may be stated to have been constant, was that it induced constipation. The stools became firm, dry, and formed. In some cases the constipation became so marked that the earth had to be discontinued. Hess then gave the earth to infants suffering from indigestion, as manifested by diarrhea, accompanied in some instances by vomiting. In these cases the earth was either added to the food, consisting of the diluted milk, or it was given by teaspoon every hour or two. Either method can be used. In sever cases of enteritis no food whatsoever was given, but merely teaspoonful doses of this preparation as often as every half hour. It may also be suspended in a little water, especially when it is sweetened by means of saccharin ($\frac{2}{5}$ grain to 1 ounce of fuller's earth).

¹ Journal of American Medical Association, April 15, 1916.

² Ibid., March 25, 1916.

³ Ibid.

⁴ Ibid., January 8, 1916.

Although Hess did not invariably achieve success with the earth, it had a greater effect on inhibiting the diarrhea than has bismuth, chalk mixture, or other drugs commonly used for this purpose. In some cases it also seemed to exert a sedative action on the stomach as judged by the fact that vomiting ceased. In no case were any harmful effects noted.

Lactic Acid Bacillus. Sufficient experimental evidence derived from both animals and man is now available to reveal in a general way the advantages and disadvantages of the lactic acid bacillus in affecting the growth of putrefactive organisms in the alimentary canal. The first point to be borne in mind in applying this remedy is that while good results may be obtained in many instances when putrefactive organisms are breaking down protein substances, digestive disturbances caused by the fermentation of starches or sugars will aggravate matters, increasing the fermentation and acidity. The second point is that a large amount of absorption of putrefactive material occurs in the large intestine, in which effects from the administrative of lactic acid bacilli are comparatively slight. In 1908, Hester and Kendall showed that it was possible, by feeding monkeys for two weeks on nothing but milk containing the lactic acid bacillus, to induce or maintain the acid reaction from one end of the alimentary canal to the other, but they also found that its efficacy was chiefly above the ileocecal valve. More recently, Rache has shown that this bacillus does not grow readily in the colon, although it seems able to survive over a considerable period of time in the small intestine, multiplying there and adjusting itself to the existing conditions.

Commenting editorially on the abuse of remedial agents, such as the lactic acid bacillus, which are used indiscriminately before their limitations and contra-indications have been determined, the *Therapeutic Gazette* says: "It is unfortunate that they are, when first brought forward, received with so much enthusiasm that erroneous conceptions of their actual value are widely disseminated, and being widely disseminated are correspondingly persistent, with the result that they are used carelessly, or distinctly abused, and, what is worse, the patient for whom they are prescribed may be also abused. The moral is that the physician must have a clear idea of what he ought to do and a definite understanding as to what his remedies can do."

Lead Acetate. A number of interesting points regarding this drug, and particularly its capacity, for acting as a slow poison, are brought out by Charteris.¹ The earliest symptom of the action of this drug noted was the presence of stippling of the red cells, that is, basophilic staining. He could not differentiate this stippling from that encountered in pernicious anemia and leukemia. The development of the blue line on the zones was observed in a patient who had received only four lead and opium pills. Another case showed it after taking 3 grains of lead

¹ Glasgow Medical Journal, December, 1915.

acetate for nine days. In one instance, the blue line resulted from the use of 42 grains of the drug, in another after 60 grains had been taken, and in still another not until 128 grains had been ingested. In a patient suffering from chronic nephritis with polyuria, albuminuria, and slight hematuria a course of treatment with lead acetate over eighteen days, with a total dosage of 108 grains, resulted in severe colicky pains in the abdomen, foul breath, and a blue line on the gums. Besides directing attention to the possibilities of slow poisoning with lead acetate, Charteris questions its value as an astringent in conditions dependent upon absorption of the drug, because of the changes to which it is subjected by the gastric juice.

Lecithin. Commenting editorially upon our imperfect knowledge in the past of the nature of lecithin, the *Journal of American Medical Association* (1916, lvi, 1029) states that physiological chemists have realized for some time that the "lecithin" of the text-book descriptions, and the "lecithin" of commerce must in many, if not all, cases be represented by a mixture of substances, unless lecithin is to be conceived of as a far more complex substance than the current hypotheses indicate. As a rule, the amount of cholin obtainable from a given "lecithin" has been too small to account for the whole of the nitrogen present. The published data range from 25 to 90 per cent.

According to McLean,¹ lecithin is represented by a mixture of two substances: rephalin, which tends to become insoluble in alcohol and a substance which remains alcohol-soluble, true lecithin. Kephalin appears to have the same general structure as lecithin, except that the base present in kephalin is beta-amino-ethyl alcohol instead of cholin, the base in lecithin. Both are monaminomonophosphatids with a ratio of N : P—1 : 1. MacLean has succeeded in isolating the "theoretical" compound described as lecithin in which the whole of the nitrogen is accounted for by the cholin present. As the *Journal of the American Medical Association* says: "Anyone who has had practical experience with the analysis of lipoid mixtures, which seem to defy almost every conventional mode of purification, will recognize a great step in advance in this achievement. It is equivalent to saying that the postulated compound lecithin is a definite chemical entity. The way is now opened for the reinvestigation of the biological properties of lecithin as an individual purified compound of recognized chemical structure."

Magnesium Sulphate. In a very interesting paper entitled "Inhibitory Properties of Magnesium Sulphate and their Therapeutic Application to Tetanus," Meltzer² discusses in a general way the phenomena of inhibition in biology, and in particular the inhibitory action of magnesium salts, the dominant action of these salts consisting in depression or

¹ Biochemical Journal, 1915, ix, 351.

² Journal of American Medical Association, March 25, 1916.

inhibition, and then takes up the *treatment of tetanus* by magnesium sulphate. The effect of this drug on tetanus is most apparent through its favorable influence on the convulsions, no other remedy, in the opinion of the author, being capable of relieving the furious symptoms to such a satisfactory degree as do the injections of magnesium sulphate. But the author believes the salt exerts more than a merely symptomatic action. "It is possible that the magnesium salts, accumulated in the lymph enter into the synaptic membrane between two neurons and thus prevent the wandering of the tetanus toxin through higher neurons and into the corresponding nerve cells."

The technic and indications for the various methods of administering magnesium sulphate in tetanus, by intraspinal injection, by subcutaneous injection by intravenous injection, and by intramuscular injection plus ether inhalation are presented. The best general plan for the treatment of tetanus is summarized as follows:

In each and every case of tetanus, 1.2 c.c. of a 25 per cent. solution of magnesium sulphate should be given by subcutaneous injection three or four times a day throughout the entire disease.

When the disease is complicated by severe tetanic attacks, 1 c.c. of a 25 per cent. solution for every 10 kg. (20 pounds) body weight (in adults) should be given by the intraspinal method.

When the disease is attended by immediately dangerous tetanic complications, from 2 to 3 c.c. per minute of a 6 per cent. solution of magnesium salts should be given then by an intravenous injection until dangerous symptoms subside or the respiration becomes shallow or too slow.

When the respiration seems to become impaired in consequence of the administration of magnesium salt by the intravenous, intramuscular or subcutaneous methods, calcium chlorid should be injected in the manner described above.

It is advisable to have at hand an apparatus of intrapharyngeal insufflation ready for use, whenever the respiration becomes slow or shallow.

Finally, the simultaneous treatment by antitetanic serum should not be neglected.

Another disease affecting the nervous system, namely, *chorea*, has been treated with magnesium sulphate, but the results in this disease did not seem to warrant a continuance of the treatment. Heiman¹ treated 5 choreic patients with repeated subcutaneous injections of magnesium sulphate, using a 25 per cent. sterile solution, 0.01 gm. of magnesium sulphate being administered per kilogram of body weight at the beginning of the treatment, the dose finally reaching 0.2 gm. of the drug to 1 kilo of body weight. In only 1 of the 5 cases was improvement noted, the other 4 showing absolutely no response as far as the psychomotor system was concerned.

¹ American Journal of Diseases of Children, August, 1916.

Magnesium sulphate was employed as a form of treatment in *dysentery* three hundred years ago, and has lately been receiving renewed attention in the non-ameboid forms of the disease. Wyatt-Smith¹ reports gratifying results as a result of his experience with magnesium sulphate in this form of dysentery during a campaign in India. His experience has been confirmed by reports from the front in the present European war, as well as from the South African war.

Impressed with the relief given a patient suffering with tetanus who had marked delirium and considerable excitability, and who recovered after treatment with magnesium sulphate, Leonard² was led to determine the value of intraspinal injections of magnesium sulphate in *delirium tremens*. A preliminary report is made on twelve cases. Lumbar puncture was performed and varying quantities of cerebrospinal fluid were removed according to the amount of pressure found, the amount varying from 10 to 40 c.c. After removal of the cerebrospinal fluid 1 c.c. for every 25 pounds of body weight of a 25 per cent. solution of magnesium sulphate (chemically pure), at a temperature ranging between 95 and 100, was introduced by means of a 1 c.c. syringe, through the lumbar puncture needle into the canal. These treatments were all given with the patient in a sitting posture. After the introduction was completed, the patient was returned to a semirecumbent position. No patient received a second treatment. All these patients required almost constant attention for twenty-four hours after the treatment was instituted, careful attention being paid to the nourishment, bladder and rectum. There were 10 recoveries and 2 deaths. Seven of the patients developed a paraplegic state in from one to two hours following the introduction of the magnesium sulphate, with lost knee-jerks, lost plantar reflexes, and relaxation of both sphincters. The return of partial function occurred in from twelve to twenty-four hours after the development of the paraplegic state, with the gradual return of the reflexes and complete motor power. Complete restoration of reflexes and function occurred usually in from thirty-six to forty-eight hours. The remaining 5 patients had weakness of the lower limbs with lessened reflexes. These patients usually suffered from retention of urine. Other constitutional disturbances noted were that the temperature rose from 1° to 3°, and the respiration became more rapid and shallow. There was also some acceleration of the pulse. Those patients who had developed a paraplegic state could only speak in whispers. In others there was no change in voice sounds.

Leonard feels convinced that the rapidity with which the delirium and restlessness subside, with restoration to the normal within twenty-four hours following this treatment, is of value in view of the little good

¹ British Medical Journal, November 27, 1915.

² Journal of American Medical Association, 1916, lxxvii, 509.

sedatives do and of the high mortality among these cases. This preliminary report is certainly sufficiently encouraging to make further results be awaited with interest.

Menthol has proved satisfactory to so many who have employed it in a variety of local inflammatory conditions, that it is not surprising to hear it recommended in the treatment of *tuberculous sinuses*. Bennett,¹ after a prolonged trial of menthol in a large number of cases, feels certain as to its efficacy and reliability in tuberculous sinuses and now makes use of this substance exclusively. Local and constitutional influences of an injurious nature are lacking. The granulations of the sinuses remain of a healthy type, discharge is rapidly reduced to a minimum, and the period of healing noticeably shortened. An added benefit is the local anesthetic action in preventing postoperative pain. The strength found most generally serviceable by Bennett is about 5 grains of menthol to 1 dram of methylated spirit. Sterilized white gauze ribbon is soaked in the solution, and, when the excess fluid has been pressed out, is immediately used as packing. The dressing need not be changed for three days.

Mercury. The frequency of *mercurial poisoning* maintains and stimulates efforts to combat this serious condition. One of the cardinal principles in the management of such cases is to continue the treatment long enough, particularly that directed to the elimination and removal of the poison from the system. Elimination in acute bichloride poisoning may continue, according to Vogel and Lee,² for periods ranging from a week to several months, during which time the escape of the drug from the body should be actively encouraged. Beside the skin and gastric mucosa, the lower bowel has come to be recognized as an important emunctory in this affection. The case of an adult has been reported by Kahn, Andrews, and Anderson³ who had swallowed between 25 and 50 grams of mercury bichloride, and, though ultimately dying from the effects of the poison, did not develop the severe colitis so frequently encountered under these conditions, which was attributed to the washing out of the large bowel with gallons of saline solution. These investigators saved the fluid so used and found, upon careful chemical analysis of almost every tissue of the body, that the largest amount of mercury was obtainable from the irrigation fluid, pointing to the value of colonic flushing for all cases.

Colonic flushing and rectal irrigation are considered by Lambert and Patterson⁴ very valuable adjuncts in their treatment of mercury poisoning. Following the usual preliminary treatment of administering the whites of several eggs and gastric lavage, these authors give the following

¹ Glasgow Medical Journal, 1916, lxxxv, 81.

² Medical Record, 1916, lxxxiv, 58.

³ Ibid., August 28, 1915.

⁴ Archives of Internal Medicine, November, 1915.

routine treatment as soon as the stomach will permit. (1) The patient is given every other hour 8 ounces of the following mixture: Potassium bitartrate, 1 dram; sugar, 1 dram; lactose, $\frac{1}{2}$ ounce; lemon juice, 1 ounce; boiled water, 16 ounces. Eight ounces of milk are administered every alternate hour. (2) The drop method of rectal irrigation with a solution of potassium acetate, a dram to the pint, is given continuously. The amounts of urine secreted under this treatment are very large. In one case, 269 ounces were passed in 24 hours on the fourteenth day of treatment. (3) The stomach is washed out twice daily. (4) The colon is irrigated twice daily in order to wash out whatever poison has been eliminated in that way. (5) The patient is given a daily sweat in a hot pack. The authors emphasize the importance of keeping up the treatment with the colonic drip enteroclysis day and night without interruption. In cases in which one single dose has been taken, after two negative examinations of the urine, on successive days, they consider it legitimate to stop the treatment. For the less severe cases, a week may be a sufficient time for treatment. But with larger or successive doses of poison, or when there is a preëxisting kidney lesion, or when treatment has been delayed, longer periods of treatment, up to three weeks, are necessary.

A successful result from treatment of mercury poisoning, according to the method suggested by Lambert and Patterson, is recorded by Cohen and Bernhard,¹ although five days had elapsed since the poison had been taken—two tablets of bichloride in half a glass of water—and although suppression of urine had been complete for at least 24 hours, before admission to the hospital. In this case the non-protein nitrogen and urea in the blood were markedly increased.

Much less common is poisoning by mercuric cyanide a very interesting case of which has been reported by Cettler and Baker.² In this instance a girl took $7\frac{1}{2}$ grains of the poison and did not receive any treatment for several hours. Recovery eventually took place, though the patient became anuric on the third day, and remained so for two days, during which time she presented the characteristic picture of severe mercurial nephritis. She was in bed for one month, and discharged as well after forty-five days. Hot colonic irrigations were a regular part of the treatment. The case is specially interesting because chemical and physical analyses of the blood and excreta were carried on for a month and a half. The non-protein nitrogen reached the high figure of 292 mg. per 100 c.c. of blood (the normal being from 35 to 45), and still recovery was accomplished. The cryoscopic findings were also noteworthy. From the normal average of 0.5600, the depression of the freezing-point was gradual as the blood retention increased. From the tenth day, when the

¹ *Journal of American Medical Association*, 1916, lxvi, 1019.

² *Ibid.*, 1916, lxvi, 1694.

urinary excretion was increasing daily, the freezing-point determinations were found to decrease steadily, the greatest depression being noted twenty-one days thereafter, namely, 0.772°C . on the thirty-first day. The authors consider this an indication that the kidneys, in resuming their function, regained their water excretory power more rapidly than their power to excrete crystalloids, retention of which they believe caused the very low freezing-point. In the present case, the clinical course was very much that of poisoning with mercury bichloride and not at all that of cyanide poisoning, which is attributed by the authors either to the small degree of ionization of the mercuric cyanid, or to the isometric structure, $\text{Hg}(\text{NC})_2$ which has been ascribed to it by some authorities.

The possibilities of doing injury by the routine administration of calomel in divided doses, instead of careful selection of patients for this treatment, is referred to by the *Journal of American Medical Association*, 1915, lxy, 1553. It is contended that it takes many hours for calomel to cause purging, and that when it is time for the first two or three doses to cause such action, many other doses on the $\frac{1}{10}$ grain plan are on the way, which may lead to protracted looseness of the bowels. For an antiseptic or germicidal action, salol is suggested as probably safer and better. Criticism is directed especially to the indiscriminate use of calomel in divided doses as a routine measure in hospitals in post-operative cases, without due regard to the condition of the stomach or intestines, and for all young children who need a laxative, or have any disturbance whatever, and for most adults suffering from intestinal disorders.

The *intravenous administration of mercury* in syphilis is recommended by Shaw,¹ who claims that the method is quick, safe and certain and free from pain, while the dose can be ever accurately measured. The therapeutic effects are said to be just as quick, and in many cases more certain and more permanent than those following salvarsan and neo-salvarsan. Availability and cheapness are also claimed for this method. Untoward effects are disclaimed, except for a low grade phlebitis which may produce obliteration of the vein used and which is in proportion to the concentration of the solution used. Shaw uses $\frac{1}{8}$ to $\frac{1}{6}$ grain of mercuric chloride for a patient of 140 to 150 pounds weight, repeated every five to seven days.

To prevent vein obliteration in the administration of mercury intravenously, Nixon² presents a method that has met with success in his hands to such an extent that the technic was used in fifty injections without obliterating a single vein. To thoroughly test the method, small lateral veins were selected, and as many as ten injections were given at approximately the same points, and yet no injury to the veins was occasioned.

¹ Medical Record, 1916, lxxxix, 823.

² Journal of American Medical Association, 1916, lxvi, 1622.

Nixon's method is to dissolve the mercuric chloride ($\frac{1}{10}$ to $\frac{1}{3}$ of a grain) in 10 c.c. of freshly distilled water which is drawn into a 20 c.c. syringe. The needle with the syringe attached is introduced into the vein, and 10 c.c. of blood are aspirated into the syringe. The mixture is then injected in the usual manner, without withdrawal of the needle from the vein. The object is to substitute the insoluble, comparatively non-irritating mercury albuminate for the soluble, irritating mercuric chloride — a substitution which takes place *in vivo* when mercuric chloride is injected directly into the vein.

The method of administering mercury intraspinaly advocated by Byrnes of the Johns Hopkins University has many theoretical advantages in its favor, and has given encouraging results. Byrnes employs an albuminate of mercury, the bichloride being added to a portion of the patient's own serum and injected intraspinaly. He found that 2 c.c. of serum completely precipitated 0.02 gm. of mercuric chloride solution, and that 4 c.c. additional serum dissolved the precipitate. Thus 6 c.c. of serum will hold 0.02 gm. ($\frac{1}{3}$ grain) of mercuric bichloride converted to albuminate in solution. Byrnes' experience indicated that $\frac{1}{50}$ grain to $\frac{1}{25}$ grain could be given safely by the intraspinal route. His technic is as follows: (1) Sufficient blood is withdrawn to yield from 12 to 30 c.c. of serum; this is centrifuged and the serum removed. (2) 1 c.c. of a solution of mercuric chloride in distilled water made to contain 0.0013 gm. to 1 c.c. is added to 12 c.c. of serum. (3) To the serum thus prepared is added salt solution up to 30 c.c. if diluted serum is to be used; if a concentrated solution is required this is omitted. (4) The mercurialized serum is heated to 56° C. for half an hour. (5) Lumbar puncture is performed with the patient in bed; pressure readings are taken, and the spinal fluid withdrawn till the pressure falls to 30 mm. The serum is then administered by gravity at body temperature, and the foot of the bed raised. Nixon's method administering albuminate of mercury intravenously already referred to, is to be compared to Byrnes' method of injecting the drug intraspinaly.

Intraspinal injections of bichloride of mercury are believed by Hunt¹ to be met with practically the same results as the administration of mercurialized serum. The advantages claimed are simpler technic, shorter methods, easier administration, and less opportunity for infection. Both methods, that of the mercurialized serum and that of the bichloride injected directly into the spinal fluid, are considered as valuable substitutes for the administration of salvarsan. Ill results are said not to occur from the direct intraspinal injection of $\frac{1}{50}$ grain of bichloride of mercury in syphilis of the nervous system. It is well to make the initial dose small, and a beginning dose of $\frac{1}{64}$ grain is recommended with a later increase to one-fiftieth.

¹ Boston Medical and Surgical Journal, June 1, 1916.

In *malaria*, Barlow¹ has employed mercuric chloride intravenously in salt solution, of such strength that 10 c.c. of solution represented $\frac{1}{2}$ grain of mercuric chloride. With four or more days interval between injections, cumulative effects were avoided. To obtain good results, each case is required to be treated individually, that is, active treatment should continue until all symptoms of malaria have disappeared, until the blood is practically normal, except for a moderate anemia and leukopenia, due to quinine therapy, and until the spleen has returned to its normal size and is not tender. Daily quinine treatment is also insisted upon.

Opium. One of the best articles published during the year on drug addiction is that of McIver and Price,² which deals with 147 carefully studied cases. Thanks to the Harrison Narcotic Law, an unusual number of patients entered the hospital, where they were under control and offered unusual facilities for purposes of observation. Many of the patients used only one drug, 38 taking morphine exclusively, and 27 using only heroin. The majority of the patients, however, used the drugs in various combinations, 21 indulging in heroin and cocaine, while 3 of the number used cocaine, heroin, morphine, and hop (opium smoking). In a study of the average duration of the various addictions, that of morphine was found to be the longest, 81 having taken morphine for an average of 99.1 years. Next in length of time came opium smoking (average 5.4 years in 43 cases), then cocaine "sniffers," with an average duration of 2.5 years, while in 82 heroin cases the average duration of the habit was approximately two years. The average daily dose of morphine taken was 15.3 grains daily, the largest amount employed by any patient being 90 grains. The heroin addicts averaged $9\frac{1}{2}$ grains daily, the largest amount used by any one patient during twenty-four hours being 30 grains. Youth seemed no bar to the institution of the drug habit: 1 first used morphine at fifteen and one at seventeen years; 5 began to use heroin when seventeen years old and one at sixteen; 5 commenced to sniff cocaine at the age of seventeen and one at sixteen; 103 were males and 44 were females; 98 were white, 2 were Mongolians, and 3 were negroes.

The frequency of stigmata of degeneration in these cases was investigated, and it was found that 40 per cent. presented to a well-marked degree one or more of the following: arrested development, such as abnormalities in shape and size of the ears and palate, irregularities in the arrangement of the teeth, abnormally shaped heads, and marked facial asymmetry. The authors, however, contend that a certain proportion of normal persons do become morphine habitues, the habit being formed through taking it over a considerable period of time for the relief of pain or insomnia.

¹ American Journal of Tropical Diseases and Preventive Medicine, May, 1916.

² Journal of American Medical Association, 1916, lxxi, 476.

The most startling statement made by the authors, and the one that should receive most careful and serious consideration by every physician, is that they "would emphasize the fact that the largest single factor in the production of morphinism has been professional medication." No less than 28 learned of the effects of the drug through its hypodermic administration by a physician or through a physician's prescription. Surely too much care cannot be exercised in employing a remedy so potent for evil, and each case should, as far as possible, be investigated to determine any signs of susceptibility or lack of self-control. The medical profession, however, is considered to have had little or nothing to do with the remarkable development and spread of the cocaine (and especially the heroin) habit of the last few years. It is curious that with the very extensive and often long-continued use of heroin in cough mixtures, cases of heroin addiction have not been more frequently traced to this source.

The vast majority of the cases of opium smoking, heroin, and cocaine sniffing were found to be acquired through association and for pleasure. These were the reasons given by all the opium smokers for their initial indulgences.

The relatively infrequent association of alcohol with the drug addiction in this series of cases is shown by the fact that 108 out of the 147 denied ever having used alcohol at all. None were confirmed alcoholics, although a number had used alcohol to excess prior to the formation of the drug habit. De Quincey's contribution to this phase of the problem is given in his own words by the authors: "I do not readily believe that any man having once tasted the divine luxuries of opium, will afterward descend to the gross and mortal enjoyment of alcohol."

Many other important phases of the subject are considered in this paper, such as the relative deleterious effects of the drugs, the symptoms of withdrawal or abstinence phenomena, the prognosis and the treatment of drug addiction, the author's conclusions as to various modes of treatment are as follows:

1. The original Lambert treatment was more satisfactory than the ordinary, gradual withdrawal.

2. The Lambert method without the free purgation (using ordinary purgation) was very unsatisfactory, patients suffering intensely and showing a marked tendency to delirium.

3. The Belladonna R. was the least important element in the Lambert treatment, having little or no greater value than other sedatives, besides having a tendency in certain cases to produce delirium.

4. Having a fixed dosage for each patient, as in Lambert's treatment, is an undesirable feature, which does not allow for individual differences; to disturb a patient every hour of the day and night is folly; and to try to blend him to a machine treatment is a very unwise procedure.

5. The best method proved to be gradual withdrawal with free purga-

tion as in the Lambert treatment and sedatives or stimulants as required in the individual case.

"Patients using daily very large doses of drugs and over long periods of time can only have the drug withdrawn very gradually, without intense suffering or danger of collapse."

With all the good accomplished by the Harrison Narcotic Law, it is still a simple matter for anyone to purchase paregoric over the counter at a drug store.

The *action of the opium alkaloids*, individually and in combination with each other, *on the respiration*, is the subject of a paper by Macht.¹ The author makes two broad classifications of the opium alkaloids based upon their action on the respiratory function. One of these includes morphine, which is the great sedative-alkaloid, although in small doses it may not interfere with efficient respiration, and may even improve it. In the other division are narcotine, papaverine, narcein, thebaine, and cryptopine, which are all distinct stimulants, and, in large doses, excitants, of the respiratory center. Codeine belongs to the morphine class, though in large doses it may also excite the respiratory center, especially in rabbits. The action of combined opium alkaloids is a summation of their individual effects. On the bronchi, narcotine and papaverine are dilators, morphine is a dilator to a less degree, codeine still less so, and the other alkaloids not at all. Morphine and narcotine seem to act antagonistically on the bronchi, their combined effect being a lesser dilatation than that produced by each of them individually. The author hopes that his findings will contribute to a more rational therapeutic use of opium and its derivatives.

The action of morphine on the heart is considered by Hering,² who discusses the experimentally demonstrated fact that morphine in large doses by increasing vagus tonicity may indirectly induce a heterotopic impulse for the heart action, that is, induce ventricular automatism. The effect of the morphine varies according as the heart is sound or diseased, the pathological heart responding more readily. Therefore, extra caution is necessary when giving morphine in cases with a tendency to abnormally located impulse production. The sudden onset of fibrillation is considered to be in many cases a reasonable explanation of an immediately fatal attack of angina pectoris, and morphine, by promoting the tendency to fibrillation, may prove a factor in the fatal outcome. He recognizes, however, that valuable aid may be obtained from the use of morphine in angina pectoris, but recommends that its dosage should be supervised with special care. The contrast is drawn between healthy and diseased organs in their reaction to drugs, the latter responding more readily to smaller doses.

¹ Journal of Pharmacology and Experimental Therapeutics, October, 1915.

² Deutsch. med. Wehnschr., September 23, 1916.

It is strange that such wide differences of opinion should still exist among surgeons as to the propriety of using opium before and after operation. Such is the case, however, and it makes one wonder if, after all, there can be a very great difference in the ultimate results, whether or not the drug is employed. An interesting contribution to this subject has been made by Davis¹ who was anxious to determine how much foundation there might be for the belief held by many surgeons that morphine, on account of its depressant effect on general metabolism is responsible for a long list of disorders appearing in the course of and following on operations, especially operations performed under general anesthesia. Davis made a study of the records of 469 patients operated upon in the Presbyterian Hospital, Chicago, and of the immunity curves (opsonic and lytic) of a series of morphinized animals. Particular attention was directed to the possible relationship of morphine to postoperative ileus (paralytic), postoperative acute dilatation of the stomach, postoperative retention of urine, and immunity. This able paper is summarized as follows:

The combination of morphine (from $\frac{1}{8}$ to $\frac{1}{6}$ grain) and atropine (from $\frac{1}{150}$ to $\frac{1}{120}$ grain) hypodermically before operations is of very little importance so far as the prevention of postoperative shock is concerned, and, in the general run of cases, plays a negligible part in the production of postoperative nausea and vomiting, tympanites, and paralytic ileus, and postoperative retention of urine. It has practically no effect on immunity. Morphine alone, preceding local anesthesia, adds nothing to the efficiency of the anesthetic, and causes postoperative nausea and vomiting in 25 per cent. of the patients; it makes the patient "dopey" and hence deprives the operator of the coöperation of the patient, which at times may be valuable. In view of these conditions, and in view of the disadvantages of imposing one powerful depressant of the medullary centers, namely, morphine on another, namely ether, the preoperative use of morphine should be abandoned. In view of the same conditions, morphine in therapeutic doses, that is, from $\frac{1}{8}$ to $\frac{1}{16}$ grain, to an adult of average size, repeated at intervals of not less than six hours, should not be denied to patients whose postoperative suffering cannot be controlled otherwise.

There is no distinct uniformity in connection with dosage. Small doses in some may produce more marked effects than much larger doses in others. Females appear to be more susceptible.

In the stomach, a rather high spasmodic hour-glass contraction is observed, rarely, but we have not seen this near the pylorus as described by others. In some instances the stomach may show no appreciable change from normal. In most cases there is more or less pyloric spasm, increased peristalsis and a decided prolongation of the emptying time.

¹ Journal of American Medical Association, 1916, lxxi, 252.

In the small intestine, morphine causes a decreased motility almost uniformly, apparently as a result of a lack of propulsion and not of spasm. When marked, it is most noticeable in the upper small bowel.

The effect on the large bowel is very variable and probably of little consequence.

Oral administration produces practically the same effect as subcutaneous injections.

The effect of moderate doses of some opium derivatives on the gastro-intestinal tract of man has been investigated by that important aid to the study of the action of drugs, the *x*-ray, by Pancoast and Hopkins.¹ This work was undertaken as the result of an observation on the gastro-intestinal motility of a patient who had a hypodermic of morphine several hours before the röntgen studies were made. There was found not only an hour-glass constriction of the stomach but also a striking retardation of the motility of the small intestine. Control studies on this patient at a later date, and when freed from the influence of morphine, revealed no such abnormalities. From their studies, which they present as preliminary, the authors draw these conclusions:

The röntgen examination is a valuable method of studying certain phases of drug effects on the gastro-intestinal tract, especially motility, and the knowledge it furnishes can be gained better by this method than by any other.

Our observations were made in a series of eleven cases given morphine and one heroin habitue. While we have been able to duplicate the phenomena observed by others, with one exception, there was a decided lack of uniformity in the effects produced in different individuals, a connection with both stomach and bowel.

Optochin. On account of the increasing use of optochin (ethylhydrocuprein), in the treatment of *pneumonia*, Smith and Tantes² direct attention to some facts relating to this drug. Optochin is an alkaloid derived from cuprea bark and in its chemical structure is closely related to quinine. While quinine clinically is methoxyveinchonin, optochin is a hydroxycinchonia. Morgenroth, in 1911, reported that he was able to protect over 90 per cent. of animals against artificial pneumococcus infection by the injection of optochin; work which has received some confirmation by others and favorable reports have been made regarding its therapeutic use in lobar pneumonia. The authors found that the pharmacological action of optochin is qualitatively like that of quinine, but differs in degree—optochin is more toxic than quinine. In view of its toxicity the authors urge caution in the clinical use of optochin, especially by the intravenous route. In their experience, the blood-pressure was lowered by its use, somewhat less than by quinine, but in association

¹ Journal of American Medical Association, 1915, lxx, 2220.

² Journal of Pharmaceutical and Experimental Therapy, 1916, viii, 53.

with greater cardiac depression. Though optochin has been advocated in local eye affections, particularly those due to the pneumococcus, the authors found that even a 2 per cent. solution was highly irritating to the conjunctiva.

Moore¹ did not obtain as large a percentage of cures as claimed by Morgenroth. Of 85 mice infected with 100 times the minimal lethal dose or less of pneumococci and treated with ethylhydrocuprein (optochin), 15 mice, or 17.6 per cent., died of pneumococcal septicemia; 13 mice, or 15.2 per cent., died of toxicity of the drug or some obscure cause, the hearts blood being sterile at necropsy (the corresponding controls invariably died of causes other than pneumococcal septicemia); 56 mice, or 66.8 per cent., survived. Of these 85 treated mice, 69, or 81 per cent., either recovered or died of causes other than pneumococcal septicemia; such, for example, as the toxicity of the drug. He has not seen any definite protective action of ethylhydrocuprein *in vivo* with an amount of infection greater than 1000 times the minimum lethal dose of a highly virulent strain.

While, therefore, optochin offers prospect of further improvement in the treatment of experimental pneumococcus infections, its employment clinically in doses sufficient to destroy the pneumococcus in pneumonia, should only be conducted, if carried on at all, with a full understanding of the possible toxic effects of the drug.

Parathyroid Gland in Paralysis Agitans. Berkeley² believes that paralysis agitans is caused by a deficiency of the parathyroid glands, and that further and more diligent study of the complicated chemical processes involved will make it ultimately possible to cure this affection in just the same way in which cretinism is cured with thyroid. While not at present claiming a cure for paralysis agitans, he considers that from 60 to 70 per cent. of the sufferers from this disease who have given the remedy a fair trial for from three to six months have been greatly benefited, and in such patients the progress of the disease has been arrested, or very materially retarded. Berkeley employs an acetic extract of the fresh bullock's glands, made by treating the ground or triturated glands with cold distilled water, filtering, and then precipitating with a very minute amount of acetic acid. This preparation is administered hypodermically in doses of fifteen minims.

Pepsin. Within a few years the employment of pepsin in all sorts of gastric disorders has declined greatly in popularity. An explanation for this is offered by the *Journal of American Medical Association* (1915, lxy, 883) in the fact that analyses of the gastric contents have revealed the constant presence of the digestive enzyme in all but the most exceptional cases of organic disease. Another reason given for the

¹ Journal of Experimental Medicine, September, 1915.

² Medical Record, July 15, 1916.

decrease in use of pepsin is the frequent lack of success of this remedy when administered by itself to demonstrate distinctly curative effects. The editorial then refers to the work of Carlson, which indicates the enormous "factor of safety" which the human organism seems to possess in respect to the pepsin of the gastric secretion. An adult normal person, if hungry, may secrete from 600 to 700 c.c. of gastric juice in twenty-four hours, while 1 c.c. of the juice will readily digest 10 gm. of finely divided boiled egg-white in three hours. From this it will be readily seen that the normal human stomach secretes pepsin far in excess of the actual needs of the gastric digestion of proteins, or at any rate in excess of what is required under ordinary conditions. Carlson remarks that this great excess of pepsin in normal gastric juice probably explains the clinical finding of great reduction in pepsin content without any evidence of impaired gastric digestion, provided that sufficient acid is present.

Among the various lines of treatment indicated in diseases of the stomach in which temporary inhibition of peptic digestion is desired, particularly in the prevention and cure of chronic gastric ulcer, Hamburger¹ especially recommends the inactivation of pepsin by complete and continuous neutralization of the gastric juice. He states that sodium chloride will prevent pepsin in aqueous solution from digesting protein. This effect is permanent, the inactivated ferment failing of reactivation by the subsequent addition of hydrochloric acid. The inactivation may be prevented, however, by dissolving the ferment in dilute hydrochloric acid. Neutralization of pepsin dissolved in hydrochloric acid alone (without the addition of sodium chloride) inhibits the ferment by the sodium chloride formed from union of alkali and acid, acting in neutral solution. Complete neutralization of the gastric juice causes similar pepsin inactivation.

In a later communication, still further developing the subject of pepsin inactivation, Hamburger and Halpern² endeavored to determine whether this inactivation of pepsin by sodium chloride was a specific phenomenon, or whether it was common to many salts. First, however, a more detailed quantitative study of sodium chloride was made, and it was found that the inhibitory effect of sodium chloride on pepsin is a quantitative reaction and diminishes with the concentration of the salt present. The authors are now engaged in investigating the clinical application of the information they have obtained to gastric diseases in which control of peptic digestion may be required. The conclusions presented in this interesting contribution are as follows:

1. The inactivation of pepsin by sodium chloride is not a specific phenomenon, but may be duplicated by any of a series of inorganic and organic salts.

¹ Archives of Internal Medicine, September, 1915.

² *Ibid.*, August, 1916.

2. The inactivation of pepsin by sodium chloride is a quantitative chemical reaction. Concentrations of 2.5 per cent. cause complete inhibition; concentrations of 0.25 per cent. cause little, if any, inhibition; concentrations of 0.1 per cent. cause acceleration.

3. Hydrochloric acid in concentrations from 0.7 to 0.9 per cent. acts as an inhibiting agent to pepsin.

4. Sodium phosphate in dilutions of 1.200 causes complete inhibition of pepsin and in dilutions of 1 to 2000 it causes partial inhibition of pepsin. The inhibition of sodium phosphate may be said to be five times that of sodium chloride and of most inorganic and organic salts, with the exception of the strong alkalies.

5. The inhibition of pepsin by various salts and alkaline substances is probably due to the hydroxyl in concentration of the solutions used.

6. The inhibition of pepsin by sodium chloride and sodium phosphate suggests the possibility of the clinical use of these salts in the prevention and cure of chronic gastric ulcer.

7. The strong neutralizing value of sodium carbonate, magnesium carbonate and calcium hydroxide suggests the possibility of their use under similar conditions.

Liquid Petrolatum. The extensive use of this oil as a laxative renders it desirable to know what differences, if any exist, there may be in the different preparations on the market. Over a year ago results were published on this subject by Bastedo¹ in brief as follows: "The results of this clinical investigation appear to warrant the conclusion that, so far as therapeutic results are concerned, the differences in the action of the three varieties of liquid petrolatum, namely, light Russian liquid petrolatum, heavy Russian liquid petrolatum and American liquid petrolatum, are too slight to be of importance. Hence, the choice between the lighter and the heavier oils and between the Russian and the American is an open one, to be determined not by therapeutic differences, but by palatability, depending on the degree to which the refinement of the oil is carried out." This subject has been further developed by Brooks² who has published some notes on the chemical character, properties, mode of manufacture and testing of oils of this class. Brooks refutes the assertion that the American preparations are composed of paraffins, instead of naphthenes and polynaphthenes, which are found in the Russian oils. He states that many American petroleum, such as most of those from the Gulf region, are like the Russian in containing no paraffin; and that, in the case of those petroleum that do contain it, the customary refining method of removing paraffin is sufficient to produce true naphthene and polynaphthene petrolatums. The history of some of these preparations would appear to furnish another example of business motives *versus* humanitarian ones.

¹ Journal of American Medical Association, March 6, 1916.

² Ibid., January 1, 1916.

Liquid petrolatum, in the opinion of Le Tanneur,¹ is an absolutely marvelous means of keeping constipation under control without resort to drastic measures. One caution, however, is to be observed in its use; the patient must be impressed with the idea that he is receiving a course of treatment which is aiming to produce a lasting cure in time. He orders 1 or 2 tablespoonfuls a day. After dinner at night or before breakfast, keeping it up for two or three weeks repeating the course as needed. Three years' experience with refined liquid petrolatum have confirmed its valuable lubricating action, and its healing influence on the minute excavations from abnormally hard feces. The author states that in autopsies of persons who have been systematically taking liquid petrolatum he has found the appendix literally stuffed with it, and adds that its presence in this way guarantees sterility from the bacterial point of view. Vegetable oils, on the other hand, are unable to serve as a lubricant for the feces until the amount ingested surpasses the dose normally saponified by the liver and pancreas. This means imposing a useless burden on these two organs, an effect which does not result when liquid petrolatum is administered.

Phenol. There are probably few poisonous drugs about which so many misleading statements have been made, particularly in regard to the appropriate antidotes, as carbolic acid or phenol. Various substances, as pointed out by Wilbert,² have been recommended as antidotes or prophylactics of phenol poisoning, for example, fixed oils, alcohol, glycerin, and the soluble sulphates of the alkalines and alkali earths. Glycerin, for instance, was early observed to lessen the caustic action of phenol on the skin, and hence it was erroneously inferred that a mixture of phenol and glycerin would be a safe, non-toxic substitute for phenol, while as a matter of fact, glycerin will not prevent the production of gangrene or the absorption of phenol. The value of *alcohol as an antidote for phenol* has been scientifically disproved by a number of investigators. Macht³ experimenting with animals demonstrated that while previous intoxication with alcohol had thereby rendered them more resistant to the effects of phenol taken afterward, Alcohol, administered to an animal after poisoning with alcohol, will aggravate the symptoms and hasten death. Wilbert found that ethyl alcohol increases the solubility of phenol in water, and makes the resulting solution more antiseptic and also more toxic. Glycerin likewise exerts no detoxicant effect on phenol.

The *efficacy of lavage in phenol poisoning* has also been studied by Macht, who states that in animals the results of this treatment depend upon the quantity of poison taken, on the time after poisoning that the

¹ Paris Médical, June 24, 1916.

² Public Health Report, April 28, 1916, p. 1016.

³ Johns Hopkins Hospital Bulletin, April, 1915, p. 98.

lavage is begun, and on the solution used for washing the stomach. He considers a strong solution of sodium sulphate to be the most useful for the purpose; while next in order comes plain water.

In discussing the merits of *sodium sulphate in carbolic acid poisoning*, the *Journal of American Medical Association*, (August 12, 1916, p. 535) questions whether the action is a chemical one, and states that it has been suggested that whatever action sodium sulphate may have as an antidote to phenol may be due to some hindrance to absorption, and possibly also to an added purgation.

Mental symptoms complicating acute tetanus during treatment by phenol injections have been reported in a case by Everidge.¹ In this case, the convulsions were controlled by chloral and bromide. Whenever the patient was allowed to come around at all, the spasms became intense. As they became less severe, the patient was treated less energetically with hypnotics. At this time the mental condition began to show a marked change. He became extremely restless and passed into a state of low, muttering delirium, with visions and hallucinations, his condition closely resembling that of delirium tremens. From time to time he attempted to get out of bed, and had to be forcibly restrained. This lasted for five days, during which time there was incontinence of urine and feces. Chloral and bromides, which had previously been adequate, now had no effect. After four four-hourly doses of half a dram of paraldehyde, however, quiet sleep was produced. After nine days the mental condition appeared normal, but on the tenth day there was a bad relapse. This lasted acutely for three days, and it was not till ten days later that the mental state again became normal.

Phenol in the treatment of wounds is advocated by Mencièrè² in a way which appears heroic, especially in view of the failure of alcohol to act as an antidote to carbolic acid. Mencièrè pours phenol freely into the wound and then rinses it out with alcohol, and is convinced that this measure has saved many men in his charge not only from amputation, but from loss of life as well. He claims that it arrests gas gangrene already under way, and acts as a life-saving measure when the wound is deep, soiled and of a bad aspect. The phenol is supposed to work down more deeply into the wounds than other antiseptics. After applying the phenol for a minute, or a minute and a half in gas gangrene, he rinses out the wound with alcohol, employing 3 or 4 liters, and then uses a mixture of 10 gm. each of iodoform, ginacol, eucalyptol, and 90 per cent. alcohol, with 30 gm. Peruvian balsam and 10 c.c. of ether.

Iodized Phenol in the Treatment of Diphtheria Carriers. With the natural difficulties opposed to the disinfection of the tonsils, and after the failure of many remedies advocated for this purpose, one accepts with

¹ British Medical Journal, March 25, 1916.

² Paris Médical, v, No. 14.

caution, albeit with hopefulness, any new recommendation that will remove diphtheria organisms from the throats of carriers. Ott and Roy¹ have employed applications of iodized phenol in 17 cases, with results sufficiently encouraging to at least indicate further trial of this treatment. Their cases consisted of carriers convalescent from diphtheria, and some that did not have diphtheria but were persistent carriers. In some of the cases repeated trials with other measures had failed to obtain negative cultures. With the iodized phenol, negative cultures were obtained after one application in 6 of the 17 cases; after the second application in 5 cases; after the third application in 2 cases; after the fifth application in 1 case; and after the sixth application in 2 cases. In 16 of the cases the treatment did not last over eleven days. The remaining case (nasal) was under treatment for twenty-one days and required nine applications to bring about negative cultures.

In all the cases reported by Ott and Roy iodized phenol (acidum carbolicum iodatum) of the *National Formulary* was used. It contains 60 per cent. phenol (carbolic acid) 20 per cent. iodine crystals and 20 per cent. glycerin. In pharyngeal cases, the tonsils, uvula and posterior wall of the pharynx were swabbed every forty-eight hours until negative cultures were obtained. In nasal cases, the entire anterior part of the nasal cavity was swabbed with iodized phenol every forty-eight hours. Cultures were always made a few minutes before the local application, which took place forty-eight hours after the previous application of iodized phenol.

No bad results were experienced. Care was taken not to allow the preparation to run over the face or drop into the larynx. The application is painful for half a minute or less until the anesthetic action of the phenol takes effect. There is a thin escharotic membrane formed at the site of application which remains for about twenty-four hours.

The authors admit they do not know the manner in which this preparation acts in ridding the throat of the diphtheria organisms so promptly. They suggest that the phenol permits the more thorough penetration of iodine into the crypts of the tonsils, the place where the organisms are reached with the most difficulty, and where they are supposed to remain for the longest time.

In the same number of the *Journal of the American Medical Association*, another method of removing diphtheria organisms in carriers is advocated by Friedberg, that of removal of the tonsils and adenoids in diphtheria carriers. In the 6 cases reported, negative cultures were obtained promptly after operation, and they remained negative. In one of these cases, positive cultures had been obtained during the fifty-seven days previous to operation. As to the time the operation should be performed, it is advisable to wait for two or three weeks after clinical

¹ *Journal of the American Medical Association*, March 11, 1916.

recovery from diphtheria. In the case of chronic carriers, no time limit, of course, is necessary.

Phenolphthalein. More than a thousand doses of this drug have been administered by McWalter¹ who considers it the most useful laxative in the Pharmacopœia. The dose for children is $\frac{1}{2}$ to $\frac{3}{4}$ grain, and for adults, 2 to 6 grains. He had given it usually in doses of about $1\frac{1}{2}$ grains, repeated from two to three times a day. After a dose of 3 to 4 grains loose motions are produced in from four to six hours, but where smaller doses are given it brings on a natural or somewhat soft and copious evacuation only once or twice daily. Its chief advantage is that it is singularly free from causing pain. It does not seem to lose its effect, at least, until it has been persisted in for a considerable time. McWalter has not observed in small doses any action on the kidneys or backache—as a result of absorption of the drug. He believes it is more active and less griping than cascara sagrada. He considers it almost an ideal laxative for pregnancy and has used it extensively in this condition. He thinks it also particularly useful in intestinal toxemia, attributing to it a certain degree of antiseptic value. In chronic mucomembranous colitis he advises its use, in dose of $\frac{1}{2}$ grain thrice daily, to prevent entrosplasm, to ease pain and to check the excessive secretion of mucus, thereby improving the neurasthenia, and the patient's condition generally.

Pituitary Gland. The importance of studying the pituitary gland in various diseases affecting the organs of internal secretion because of the interrelationship of these different structures is emphasized by Try,² who investigated the histological changes occurring in the pituitary gland in 8 cases of diabetes mellitus associated with demonstrable disease of the pancreas, 3 cases of acute pancreatitis, 1 case of carcinoma of the pancreas, 2 cases of myxedema, 1 case of cystic goitre, 1 case of Addison's disease, and 2 cases of hypertrophic thymus. The most important result of this study was the demonstration of definite histological changes in the anterior lobe of the pituitary body in the cases of diabetes. These changes consist in the presence of adenomatous masses of eosinophile cells, colloid invasion of the anterior lobe, and areas of cellular degeneration. In the cases of acute pancreatitis and carcinoma of the pancreas, the histological changes in the pituitary gland are absent or slight. In myxedema, there occurs in the pituitary an increase in weight resulting from an increase in the connective-tissue elements and a hyperplasia of the chief cells. In goitre, there is a hyperplasia of the chromophile cells, especially of the eosinophile cells, and an increase of colloid material in the enteroglandular cleft. No histological changes were observed in the pituitary gland in the case of Addison's disease or in the cases of hypertrophied thymus.

¹ Lancet, November 20, 1915.

² Quarterly Journal of Medicine, July, 1915.

While extracts of the pituitary gland have been frequently recommended as *peristaltic stimulants*, it must not be overlooked that opposite effects have at times been encountered experimentally in animals. Haskins,¹ refers to the depression observed by Shamoff in applying extracts of the gland to isolated loops of rabbit intestine, and gives his own experience with intravenous injections of pituitary gland on the small intestine. Dogs were anesthetized and the dorsal portion of the spinal cord destroyed. A section of the intestine was immobilized (Trendelenburg technic) and a recording lever attached. In 5 cases out of 6 a clean-cut depression of tonus and peristalsis occurred. Commercial "pituitrin" was the extract used. Whether or not the process of preparing the extracts for the market affects the results, Haskins considers that each lot of the product should be tested by the manufacturer and its effects on peristalsis stated on the label of the container.

In *bronchial asthma*, Warfel² observed marked improvement in 6 cases treated with a preparation of the anterior lobe of the pituitary gland. Two and one-half grain tablets were administered orally four times a day. Two considerations prompted this method of therapy: In the first place, Warfel was impressed with the encouraging results following the use of this portion of the gland in certain types of cases of physical underdevelopment and of disturbed metabolism, supposedly due to a defect in the anterior portion of the pituitary body. Secondly, the striking results obtained in controlling attacks of asthma by the hypodermic use of adrenalin chloride suggest that the asthmatic symptoms may depend upon deficiency in secretion on the part of the adrenal gland. If this were so, Warfel reasoned that the administration of the desiccated anterior lobe of the pituitary gland might promote the secretion of the adrenal gland and thereby relieve the patient's symptoms.

However, when one realizes how evanescent are even the most satisfactory results from the use of adrenalin in controlling asthma, this latter line of reasoning on the part of Warfel would need much more clinical support before carrying much conviction as to the value of the treatment of asthma with the anterior lobe of the pituitary body.

Reports of value of preparation of the *pituitary gland in obstetric practice* continue to accumulate. Friedman³ comments on the favorable effects of pituitrin in placenta previa in his own experience and in that of Hanah and Meyer, and of Madill and Allen. He prefers small to large doses of the drug.

O'Connor,⁴ advocates the use of pituitrin in cases of inevitable and incomplete *abortion*. The administration of 1 c.c. of pituitrin hypodermically every three hours, if necessary, in combination with a reliable

¹ Journal of American Medical Association, 1916, lxvi, 733.

² Indianapolis Medical Journal, July, 1915.

³ New York Medical Journal, October 2, 1915.

⁴ Lancet-Clinic, October 2, 1915.

preparation of ergot by the mouth, will, according to O'Connor, aid nature in removing the contained products and in preventing complications. In a large number of cases of *menorrhagia* and *metrorrhagia* not dependent upon growths or overgrowths in the uterus, Bandler¹ says he has rarely failed to benefit the patients, administering one ampoule daily or on alternate days for weeks at a time.

Jamieson² asserts that he has been able to reduce his proportion of instrumental deliveries from 28 to 10 per cent.

More conservative than many of the contributions to the subject of the use of pituitrin in *labor* is an article by Foulkrod,³ in which he discusses the various causes for which pituitrin is advocated in labor. His experience has not yielded the frequent brilliant results claimed by some, and he is much impressed with the possible dangers attending its use when incautiously given. In uterine inertia due to a tired muscle after a long first stage, when the contractions have been good, if a complete rest is secured before the drug is administered, and if the head is out of the cervix and in the pelvis, and if the family objects to the use of ether and forceps, Foulkrod considers that pituitrin may be used cautiously. He insists that pituitrin must not be used unless the presenting part is definitely engaged in the pelvis and the largest diameter has passed through the plane of the inlet, and then only if the outlet has been carefully measured for any contraction of the transverse diameter. He asserts that pituitrin is at present going through the same class of experiments as ergot did before it came to have a definite settled use, and contends that it yet remains to be proved that pituitrin is any safer than ergot used in the same proportionate scale of dosage.

Commenting on the *abuses and dangers of pituitary extract in labor*, Bandler⁴ emphasized that this method of treatment, like the use of forceps in labor, is attended with grave risk; for example, rupture of the uterus. All the indications and contra-indications are observed. He refers to the dangers that may attend the use of even small doses, and states that if used in what is considered the average dose by many practitioners, serious injury is bound to result. Bandler never uses more than a third of an ampoule at the first hypodermic injection; occasionally, when necessity demands, going as high as one-half an ampoule. The effect of the extract of the gland he has found to be very transitory, lasting only half an hour. Bandler in some instances has repeated the dose every half hour, giving eight, ten, twenty and even more injections in a large number of cases, with the result that the application of forceps has been avoided. Properly used in suitable cases Bandler warmly advocates the use of this remedy.

¹ Medical Record, October 9, 1915.

² New Zealand Medical Journal, October, 1915.

³ Therapeutic Gazette, May 15, 1916.

⁴ New York Medical Journal, October 30, 1915.

Whatever position the future may assign to the value of the pituitary gland in obstetric work, it is much to be desired that its exact status should be most carefully studied, and its employment regarded with due caution and a full knowledge of all the data at present available.

As time goes on, our knowledge of the functions of the pituitary gland is constantly increasing, and the special functions of the anterior and posterior lobes respectively are becoming more definite. A very valuable and, from the therapeutic stand-point, quite suggestive paper on the *functions of the anterior lobe* has been contributed by Coetsch.¹ This paper confirms previous work indicating the association of the anterior lobe with physical and sexual development. Coetsch fed young male rats with extract of the anterior lobe of the pituitary body and observed a definitely stimulating effect upon the growth of the animal body in gain in weight and in its general appearance of vigor. Descent of the testicles took place earlier, and they appeared larger and more vascular than the testicles of a control animal which, at the start of the experiment, had been of the same size. That is, the use of the anterior lobe extract shortened the period of complete sexual development by one month, or one-third. The posterior lobe extract failed to produce a stimulating influence in any way comparable to that exerted by the anterior lobe extract.

Experiments were also conducted to determine the effects of the anterior lobe on pregnancy. Female rats fed as were the male ones exhibited early developmental changes in the uterus, ovaries, and tubes, and a male and female rat receiving the anterior lobe bred at the age of three and one-half months, much earlier than is ordinarily the case. How much benefit will be derived from the administration of the anterior lobe to human beings in overcoming retarded physical and sexual development remains to be seen, but should be thoroughly tested out. It is interesting that, in the experiments, the physiological effects of the gland were apparently not interfered with by oral administration.

Pollen Toxin in the Treatment of Hay-fever. The treatment of hay-fever or pollinosis has been successfully established in the past two years, according to Howe.² Some confusion still exists regarding the preparation of the toxin; how long before the onset of the hay-fever symptoms should be initiated; and the relation of skin reactions to immunity. But more or less successful results are being attained regardless of how the toxin is prepared or whether the injections are begun before or after the onset of the symptoms. The attainment of absolute immunity for succeeding years is a question that only time and a wide experience can positively establish.

During the season of 1915, 47 cases of hay-fever came under Howe's

¹ Bulletin of Johns Hopkins Hospital, February, 1916.

² Long Island Medical Journal, May, 1916.

care. Forty-two of the 47 cases were more or less benefited or relieved by the injection of a pollen toxin. Three received absolutely no relief from the treatment, and 2 discontinued it for various reasons before results could be expected. Of the 42 favorable cases, 23 were practically rendered immune, except for two or three outbreaks that lasted for twenty-four to forty-eight hours. These cases were entirely free from any uncomfortable symptoms after immunity was established except for these few short outbreaks. The remaining 19 cases were relieved to such an extent that none were obliged to leave their occupations or to leave the city. Most of them were entirely free from symptoms for a greater part of the time. The rest of the time their symptoms were annoying but not distressing, and their hay-fever season was made not only very mild but much shorter. Treatment was begun before the onset of symptoms in 16 cases. Of these, 10 were entirely immune throughout the season, developing no symptoms. Twenty-six cases came under treatment after the beginning of their hay-fever. Eleven of these were practically free from symptoms after immunity was established; while 15 were subject to several short attacks with intervals of absolute freedom, or to a persistent mild nasal stuffiness with no rhinorrhea, sneezing or conjunctival itching or burning. By skin tests Howe has found that most of these cases were sensitized to two or more pollens, and the persistent mild nasal symptoms were due to a slight sensitization to pollen of which he had no toxin.

Wilson¹ gives a conservative estimate of the value of pollen solutions and advise caution in their use. He treated 26 cases with pollen solutions and 22 with calcium chloride. Pollen solutions for therapeutic use should be prepared and used with great care and understanding. When improperly prepared or used, there is danger of serious, if not fatal, reactions. Multiple sensitization is a frequent phenomenon in hay-fever subjects, and its existence may account for many failures in the treatment by means of pollen solutions. The treatment of hay-fever by means of calcium salts rests largely on empirical observations, but from the limited data at hand, if the doses are sufficiently large, and prolonged through a more or less extended time, a large percentage of patients will receive material benefit. It is possible that vernal cases yield more readily than autumnal cases. The administration of calcium salts is without danger to the patient and may be undertaken by any intelligent physician. It requires neither a careful laboratory technic, nor any special knowledge for its employment.

Potassium Iodide. THE EFFECT OF POTASSIUM IODIDE ON THE LUTIN REACTION. A very important precaution in the employment of the luetin reaction for syphilis has been pointed out by two authorities. Sherrick² reported that "a positive pustular or nodular luetin reaction can be

¹ Laryngoscope, June, 1916.

² Journal of the American Medical Association, 1915, v, 404.

obtained in 99 per cent. of all persons irrespective of the presence of syphilis, by the administration of potassium iodide, either simultaneously, or shortly before or after the intradermal test. Other substances, such as agar and starch, when injected intradermally, will give a similar reaction when potassium iodide is administered." Other drugs containing iodine were found to have a similar effect. This work has been corroborated by Kolmer, Matsunami and Broadwell¹ who present the following conclusions:

1. Well-marked positive luetin reactions were observed among a group of healthy non-syphilitic persons following the administration of potassium iodide.

2. Similar results were observed among non-syphilitic persons suffering with various other diseases.

3. Somewhat severe reactions were observed following the intracutaneous injection of 0.1 c.c. of 0.5 per cent. agar-agar.

4. The strongest reactions were observed when the luetin was injected during or immediately after the ingestion of potassium iodide.

5. Positive luetin reactions were observed among normal non-syphilitic persons as late as one month after the ingestion of large doses of potassium iodide.

6. In some instances the ingestion of potassium iodide causes the site of a former luetin reaction to develop inflammatory phenomena progressive to pustulation.

7. Similar, but less marked, reactions to luetin and agar were observed among guinea-pigs and rabbits following the oral administration of potassium iodide.

8. Accordingly, a positive luetin skin test has little value in the diagnosis of syphilis among persons who are taking or have recently taken potassium iodide. The amount of iodide capable of producing these reactions varies considerably; also the length of time following the ingestion of iodide when this reaction to luetin may follow. For these reasons physicians should very carefully rule out the possible influence of iodides before conducting the luetin skin test.

Quinine. An important investigation to determine the relative therapeutic value of the more important cinchona alkaloids and their derivatives has been conducted by MacGilechrist.² The five alkaloids and two quinine derivatives studied in the order of their therapeutic value was determined to be as follows: (1) Hydroquinine hydrochloride; (2) cinchonine sulphate; (3) quinine sulphate; (4) quinidine sulphate—the first three for all practical purposes being of equal value, the order given showing any possible relative degrees of superiority; (5) optochin (ethylhydrocuprein) hydrochloride; (6) cinchonidine sulphate; 7) quin-

¹ Journal of the American Medical Association, 1916, lxx, 718.

² Indian Journal of Medical Research, Calcutta, July, 1915.

oidin. Regarding unpleasant by-effects of these alkaloids, buzzing in the ears was most frequently associated with quinine and quinidine; diarrhea with cinchonine if administered for over a week; and nausea with quinoidin. Cinchonidine, even in large doses, caused no unpleasantness of any kind.

The first forms of the parasites to disappear from the peripheral blood are the sporulating forms, next, small rings, and still later the half-grown parasites become rare and disappear. The last forms discoverable are full-grown shizonts and gametes.

How small a dose of quinine is required to free the peripheral blood of sexual parasites and possibly to check the production of gametes is demonstrated. The minimal lethal doses for the vulnerable stage of the benign tertian, malignant tertian, and quartan parasites being respectively, about 0.1, 0.15, and 0.2 gm. per 70 kilogram of patient's weight. The dosage being sufficient, the average number of hours required to cause a disappearance of parasites from the peripheral blood is roughly proportionate to the duration of the life-cycle of each parasite, the number of hours in any individual case depending on the period required for the parasite to reach a vulnerable stage in its developmental cycle. To a patient in whom gametes have developed, it would appear that quinine should be administered daily for a period equal to the life-span of the individual gamete if there is to be any prospect of curing and disinfecting that patient. Ordinary doses of cinchona alkaloids are considered by MacGilchrist to have little influence on crescents when once these are fully developed in the peripheral blood, but they apparently check the production of crescents if administered before these bodies have appeared in the peripheral blood, and greatly shorten the period during which these bodies, having made their appearance during treatment, can be found in the peripheral blood.

Improvements in the manufacture of cinchona derivatives for use in malaria suggested by this investigation are: (1) To obtain a bark containing as little quinidine as possible; (2) to extract quinine for use as such and for the manufacture of hydroquinine, and (3) to issue the remaining alkaloids as residual alkaloid, which should contain as little quinidine as possible, but have a high percentage of quinine, cinchonine, and quinidine combined.

In the specific treatment of *malignant or pernicious malaria* during the severe attacks, Daso¹ urges the *intravenous administration of quinine*. The single dose advocated should not exceed 10 grains, and not more than 30 grains of quinine hydrochloride should be given intravenously within twenty-four hours. Twenty grains at a dose often produce considerable shock, dizziness, nausea, etc., and a dose of 50 grains has killed in several instances. Bass has known of several cases in which 100 grains

¹ Journal of American Medical Association, August 14, 1915.

or more of quinine had been administered during the last twenty-four or thirty-six hours before death. Usually, this destructive treatment is continued because the patient continues to get worse. The symptoms attributed to a continuation of the reproduction of malarial plasmodia are usually due to the quinine. Examination of the blood of such patients usually shows few organisms, and most of them are dead or dying. The necropsy fails to reveal sufficient parasites to cause death, and the inference is that not they but the quinine is responsible.

In *malarial hemoglobinuria*, quinine, according to Bass, is both useless and harmful. Useless because in the process of hemolysis the cells containing the plasmodia are more certainly and extensively affected than the normal cells, and the parasites becoming exposed to the plasma are promptly destroyed by it. Quinine may be harmful in cases of hemoglobinuria because it tends to promote hemolysis, or to precipitate attacks of hemoglobinuria in otherwise susceptible individuals.

The apparent innocuousness of the large amounts of foreign protein in the blood stream occasioned by the presence of so many parasites, which Bass estimates may constitute a pint or more of the plasmodia, leads him to believe that the protoplasm of the parasite is of very low toxicity.

As a *dressing for wounds* the value of solutions of *quinine hydrochloride* have proved most effective and at the same time quite free from danger when properly employed. Taylor¹ has had considerable experience with a 1 per cent. solution of quinine hydrochloride in cold boiled water, and the same solution was used as an instillation. Some of his patients received a continuous drip of $\frac{1}{10}$ per cent. solution of quinine hydrochloride with the addition of $\frac{1}{10}$ per cent. of hydrochloric acid, or of 1 per cent. of alcohol. About 125 cases were treated, the majority being received within forty-eight hours after the injury. Seventy per cent. had been heavily infected with the gas bacillus, and all with staphylococci, streptococci, and the usual flora or putrefactive bacteria. About one-half the cases had open fractures of the long bones of the arm or leg. Most of the wounds treated with the solutions of quinine ran a favorable course. They rapidly improved in appearance, sloughs disappeared, the putrefactive odor often vanished within twenty-four to forty-eight hours, while the amount of discharge greatly lessened, and red vascular granulations made their appearance with surprising rapidity. Other forms of dressing gave much less favorable results.

It is to be hoped that the very satisfactory results claimed for quinine and urea hydrochloride as a local anesthetic may receive general confirmation. This drug is a double salt of quinine and urea, a carbamided quinine and 11 per cent. of urea. It possesses the primary requisite of a local anesthetic in being relatively non-toxic, readily soluble in water, and in not decomposing on boiling. Amstutz² uses a freshly pre-

¹ British Medical Journal, December 15, 1915.

² New York Medical Journal, October 2, 1915.

pared solution of from 0.125 to 0.25 per cent. strength, which he says may be employed freely without causing untoward physiological or toxic symptoms sometimes met with after the local administration of cocaine and other dangerous drugs. To insure success, anesthetization with this drug must be accompanied by all the necessary details as to asepsis and manipulation, a disregard for which is responsible, in Amster's opinion, for many failures. His experience covers six years, and he is most gratified with his results. Postoperative pneumonia, a dreaded complication of general narcosis, is said to be absolutely unheard of with the use of quinine and urea anesthesia. Amster's group of cases covers a large field of surgery, including inguinal herniotomy, appendectomy, colostomy, cholecystotomy, salpingo-oöphorectomy, suprapubic cystotomy, tenorrhaphy, amputation of fingers and toes, rib resection for empyema, operation for pedunculated submucous uterine fibroid and polypus (vaginal route), laceration of cervix and perineum, urethral caruncle, inguinal and cervical adenitis, thrombosis of the internal saphenous vein, varicocele, hydrocele, enlarged prepuce, gangrene of testicle and epididymis, periprostatic abscess, ischiorectal abscess, hemorrhoids, carbuncle, epitheliomata of face and scalp, alveolar abscess, sebaceous cyst of scalp, lipomata, foreign bodies of hand and foot, ingrowing toe-nails, exostosis of tibia and fibula, bursitis, abscess and benign tumor of the breast, abscesses in other parts of the body, lacerated wounds, etc. In this series of cases quinine and urea hydrochloride was used exclusively with the exception of a short time during two operations: one, the removal of a large ovarian cyst, the other, an embedded retrocecal appendix.

Quinine and urea hydrochloride injections in *hyperthyroidism* are favorably recommended by Watson¹ who has employed this form of treatment over 400 times. He believes the greatest field of usefulness for the injection will be found in those cases of beginning hyperthyroidism not severe enough to justify operative treatment, and as a preparatory measure to partial thyroidectomy in chronic cases of toxic goitre too ill to warrant any form of immediate operative procedure. The method is recommended only to relieve hyperthyroidism and not to remove the goitre. The injections should be carried on in a hospital by men skilled in goitre work. The best results are obtained by keeping the patient in bed in a hospital several weeks while giving the injections, the length of time depending on the severity of the symptoms and the response to treatment. The indiscriminate use of quinine and urea, in the hands of one not familiar with the low threshold to stimuli possessed by the average case of toxic goitre, is liable to produce alarming symptoms of hyperthyroidism, which might result disastrously.

Radium. The danger of careless and indiscriminate use of an agent as powerful and as capable of profound systemic disturbance as radium is

¹ Southern Medical Journal, May, 1916.

pointed out by Newcomet,¹ who discusses its local and internal use. No discredit is given to the value of radium products in treatment, but "like all other materials used in our medical arts, the results are in proportion to the skill employed in their use." Their value as therapeutic agents has by no means been established. In spite of this, they are being employed throughout the country for the relief of distressed individuals by persons having little comprehension of the consequences. Newcomet considers it fortunate that the dosage employed has often been small, and the baneful effects in many cases inconsequential. In these cases, the small doses probably also accounted for failure to obtain expected results. As an argument in favor of establishing a central station for determining the value of radium offered for sale, and as a plea that those using radioactive products should familiarize themselves to some extent with physics, the following incident is related: A dealer had two tubes of radium for sale which he stated had been originally purchased from a well-known chemical house, the price being \$400 to \$1400. Tests were made, and it was found that the amount was frightfully small compared with the price asked. The tubes were then sent to Washington where it was determined that the value of the radium in the tubes was 40 centt and \$30 respectively.

Among the most encouraging results obtained in treatment by radium are those reported by Kelly and Burnam² who feel convinced of its great value in *cancers of the cervix uteri and vagina*, and anticipate even better results as time goes on. Even in those cases that are not cured, improvement is often sufficient to be a great recommendation for its use. Every inoperable cancer of the cervix uteri or vagina, provided general metastasis is not evident, is considered to stand a chance of at least 1 in 4 of cure by radium treatment. Radium and operation in operable cases is believed to hold out great promise of success. Both hysterectomy and radiation are advised in clearly operable cases. In borderline cases they advise the use of radium, as the permanent cures from this group are not great. The authors are emphatic in asserting that radium can and should be used in these cases without any local or general injury to the patient.

Encouraging results from radium treatment of *cancer of the pelvic organs* is also reported by Schmitz.³ His conclusions are in part as follows: Inoperable cancers that are not far advanced so that cauterization is not contra-indicated, yield satisfactorily to radium therapy. Advanced, inoperable and recurrent cancers are ordinarily refractory toward the radium rays. Any improvement is at least very temporary. The patients treated with the rays after removal of the organs have done well, although the time elapsed since the treatment averages eight months. Patients suffering from cancer should be treated surgically and then

¹ Therapeutic Gazette, February 15, 1916.

² Journal of the American Medical Association, November 27, 1915.

³ Ibid., November 27, 1915.

radiologically, and if surgery is contra-indicated they should receive radium treatment which at least relieves the subjective symptoms and often the objective ones. The time elapsed since the commencement of the radium treatment in all the cases enumerated is too short to permit definite opinion as to the remote results of radium treatment. Clinical and histological studies enable us to pronounce the radium rays a valuable addition to the therapy of cancer. It will require years of constant observation to demonstrate such results as anatomic cures. The same measure that is applied to establish the efficacy of surgical procedure in cancer treatment must certainly be employed in radiotherapy.

In the treatment of uterine cancer, Flatau¹ holds the usual position of advocating exclusive radiotherapy. He has done no operation for cancer of the uterine cervix since 1913. The proportionate number of women still living and cured under radiotherapy alone is larger than he could ever report before with abdominal operations for cancer of the cervix. It is claimed to be now beyond question that an incipient cancer focus can be destroyed by radium without leaving a trace. However, certain experiences have suggested the possibility that although the primary focus may thus vanish and leave no trace behind, metastases develop at remote points, far beyond the scope of the rays. Time alone can tell whether radiotherapy will oust surgery from the arena of treatment.

In discussing radium, Moriarta² emphasizes the fact that the gamma rays are the ones most valuable therapeutically, and, in treatment, our problem is to get the greatest amount of these rays in any given places. This will depend upon the intensity (amount of radium used), the manner of filtration, and the period of time of exposure. The intensity of an application is greatly augmented by what is termed "cross-firing," that is, the focusing of gamma rays from several sources upon a given district. The burying of a tube will also increase its efficiency many times. Moriarta presents a glowing description of the values of radium in treatment. Anemia, metabolic processes, the elimination of carbon dioxide, urea and uric acid, the diminution of the viscosity of the blood, the increase in urinary secretion, improvement in appetite and digestion, relief of gouty manifestations and neuritis, the lowering of blood-pressure, are among the conditions which he claims may be greatly and favorably influenced by radium treatment.

Salicylates. That the usefulness of salicylates in *acute rheumatic fever* continues to be demonstrated is upheld by Beverley Robinson³ who maintains that despite all our advances in knowledge during the past few years, we have not improved on the salicylates in the treatment of this disease. Though having limitations, inasmuch as they are no specifics, and though possessing objections, no other agent relieves the acute pain of

¹ Centralblatt f. Gynakologie, Leipzig, August 28, 1915.

² Medical Record, March 4, 1916.

³ Ibid., January 1, 1916.

the affected joints so rapidly and considerably. In addition, they possess antipyretic value when the fever is high or threatens to become so. When oral administration of the salicylates is contra-indicated, resort may be had to intravenous administrations or rectal injections. With proper technic, 20 grains of chemically pure sodium salicylate may be used, repeated within eight or twelve hours. Robinson, however, prefers rectal injections to the intravenous method. Following a soapsuds enema, as much as 2 drams of salicylates may be given in this way, dissolved in a few ounces of water, with the addition of 15 minims of tincture of opium, and the injection may be repeated in twelve hours. The amount of salicylates to be given intelligently will depend upon the view we have of their action and of the effects produced. To some who regard them as specifics in rheumatic fever, frequent doses are essential to obtain good results. To others, who still regard them only in a measure as specifics, such doses are not desirable, and the best results are obtained when 10 to 20 grains of the soda or ammonia salt are given by the mouth every three or four hours. The author shares the later view and also believes it well to combine with their use an equal amount of bicarbonate of soda, either with the salicylates, or between the doses of salicylates. He prefers the ammonium salt to the soda in the same dose. When the joint-pains have diminished, he greatly prefers salicin to any other salicylate. Whenever the heart is weakened or slightly dilated and a murmur exists, this alkaloid is considered especially valuable. He prefers in the treatment of rheumatic fever, as the best combination internally, salicylate of ammonium 5 to 10 grains, phenacetin 1 or 2 grains, caffeine $\frac{1}{2}$ to 1 grain, every two or three hours in two capsules at the beginning of an attack, later, every three or four hours.

The administration of *salicylates in childhood*, according to Bendix,¹ should be based on the same principles as in adults. His method is to give the drug three times a day till free perspiration is secured. Their action is enhanced by a warm bath followed by wrapping the child up dry and warm. In the severer and the irregular forms, the salicylates may fail, and no aid is to be expected from them in cardiac complications. He has never seen any serious unfortunate effects from them in children, so that large doses can be given without apprehension.

STRONTIUM SALICYLATE. This drug in the opinion of Blankenhorn² has enjoyed a therapeutic reputation unsupported by any satisfactory foundation. In the hope of finding out whether strontium salicylate, taken internally, differs therapeutically from any other salicylate, it was administered in the wards of the Lakeside Hospital, Cleveland. It was used in the treatment of rheumatic fever, tonsillitis, and endocarditis mainly, in the same wards, and practically under the same conditions

¹ Medizinische Klinik, October 24, 1916.

² Journal of American Medical Association, 1916, lxxvi, 331.

obtaining when observations were made on the toxicity of other salicylates as reported by Hanzlik.¹ In all cases the patients were above twelve years of age, and the drug was given in 20-grain doses, combined with an equal amount of sodium bicarbonate, hourly, until symptoms of intoxication appeared. The bicarbonate was added, since this is the routine practice of the service with sodium salicylate, and was, therefore, necessary for purposes of comparison. The extremes of the toxic dose of strontium salicylate obtained were 80 and 500 grains, the mean dose 180 grains. The mean dose giving marked relief of pain was 260 grains.

Comparison of Blankenhorn's figures for strontium salicylate with those of Hanzlik for other salicylates reveals great similarity between the effects of strontium and other salicylates. The authors conclusions are:

1. The mean toxic dose of strontium salicylate is the same as that for sodium salicylate.
2. Strontium salicylate produces the same gastric and other toxic symptoms produced by any salicylate.
3. It is no more effectual in relief of pain.
4. It is not so convenient to give as are the more soluble salicylates.

ACETYSALICYLIC ACID (ASPIRIN). In administering drugs it is not often that one has to seriously consider the matter of idiosyncrasy, but in the case of aspirin unfortunate results have occurred so often that it would seem wise to make it a habit to instruct patients, and especially certain types of patients to begin treatment with a dose much smaller than usual to determine whether any susceptibility to the drug exists. The deleterious effect usually occur very rapidly, often within a half hour or less, so that little time is lost in postponing full treatment. Seventeen cases of aspirin poisoning from the literature, and three from his own practice, are reported by Kereker,² all the result of therapeutic administration of the drug. The doses ranged from 0.3 to 1 gm. and the pathologic reaction occurred always at the first dose, and independently of the amount taken. Subsequent doses were not always associated with untoward results. Edema was a constant phenomena, the lids and face swelling, the skin puffing up sometimes down as far as the chest. In some of the cases there was also a tendency to urticaria, near the swollen patches or more diffuse. In some of the cases the edema involved the mucosa of the nose and pharynx; in two cases there was edema of the larynx. The edema rapidly reached its height and subsided as a rule in twenty-four hours. Some instability of the vasomotor system is considered responsible for the trouble, but no record of family idiosyncrasy was discoverable. Some favorable factors were probable in certain cases, application of local heat, fear of poisoning, a preëxisting infection or other coöperating cause. He is inclined to place considerable stress on the emotional factor in those with an unstable vasomotor system.

¹ Journal of American Medical Association, March 29, 1913.

² Hygeia, Stockholm, Lxxviii, No. 4.

The effects of the salicylates on the uric acid content of the blood have been investigated by Denis.¹ In those patients whose blood gave non-protein nitrogen values but little above normal, the administration of salicylates had no effect on this fraction. In two or three cases, however, whose non-protein nitrogen was unusually high, a considerable diminution of the fraction took place after the administration of the drug. His findings also indicated that as soon as the drug is withdrawn the accumulation of waste products recommences, which is in accord with the long known fact that after the administration of salicylate is discontinued the output of uric acid in the urine is frequently diminished below the level at which it stood previous to giving the drug. From the foregoing results the increased output of uric acid following salicylate medication seems to be due to a lowered threshold value of the kidney, not only for uric acid, but in all probability for other waste products as well. Such being the case, it may well be that the beneficial effects resulting from the use of salicylates in acute rheumatic fever may, in part at least, be due to a power possessed by these drugs of increasing kidney permeability, thereby facilitating the rapid and more or less complete excretion of the as yet unknown toxins which produce symptoms of these diseases.

The effects produced by the ingestion of sodium salicylate on the urine, feces, blood, and on the respiratory exchange of three men were studied by Denis and Means.² In the case of two normal men the administration of large doses of sodium salicylate, up to 6.6 gm. per day, produced an increase in the excretion of nitrogen, phosphates, and uric acid. In one case, this increased nitrogenous metabolism was accompanied by an increase in the basal metabolism and symptoms of salicylate intoxication (such as ringing in the ears). In the other case, a much greater increase in the urinary excretion of nitrogen (which extended throughout the after-period) was observed, but there was no increase in the basal metabolism, and no symptoms of intoxication. In one mildly septic individual results similar to those secured with the second normal man were obtained. No change in the respiratory quotient occurred in any of these subjects.

SALICYLATES IN SCARLET FEVER. The many analogies between scarlet fever and acute rheumatism seem to have been confirmed by the benefit from salicylic medication in the experience of F. Ramond and G. Schultz³ with scarlet fever in soldiers. They give 6 gm. a day, occasionally even more, fractioned throughout the day and night, commencing as early as possible, and keeping it up until the fever and general symptoms have subsided. This is usually within three days, but, to be safe, the drug is kept up for another two days. It is resumed again the fifteenth day, the

¹ *Journal of Pharmacology and Experimental Therapeutics*, October, 1915.

² *Ibid.*, June, 1916.

³ *Bull. de la Soc. méd. d. hôp. de Paris*, 1916, xxxii, 866, cited by the *Journal of American Medical Association*.

dose being reduced by 1 gm. a day. This wards off the complications which are so liable to develop from the fifteenth to the twentieth days, especially tonsillitis and nephritis. If the heart gives symptoms of trouble, the salicylate should be given more cautiously and its elimination in the urine supervised even for this. The mortality under this treatment dropped to 0.25 per cent. and complications were exceptional and mild.

Saline Solution. Hot saline solutions in the treatment of *sciatica*, and of *neuritis* of other peripheral nerves. The injection of alcohol to relieve neuritis affecting the peripheral nerves has been abandoned by Gordon¹ because of clinical and experimental data demonstrating the possibility of direct damage of alcohol to the nerves. Instead, he has employed saline injections, and, after trying out various temperatures, concluded that solutions of high temperature, give better and more lasting results. The technic of the injections, the location in the involvement of different nerves, and the frequency of the treatment are described by the author. Good temporary results are reported, but the time since treatment was instituted has not yet been sufficient to allow one to claim permanent cures. He concludes: "I am able to speak of great relief and of the superiority of this method over all others known to me including surgery. I am warranted, therefore, to recommend it in the most emphatic manner."

Silver Nitrate. In the treatment of *diarrhea* of all sorts rectal injections of silver nitrate solution are strongly recommended by Rakus.² He employs 25 gm. of a 2 per cent. solution of silver nitrate in half a liter of tepid water. The patient is placed in the knee-elbow position, and the enema is retained as long as possible, this being facilitated by squeezing the parts to retain the fluid. In the severe and febrile cases, he gives two of these enemas a day. One or two enemas often meet the indications, in other cases eight or more are required. No water is permitted during the entire course beyond a swallow of hot Russian tea every half hour the first day. The second day a little thin soup is permitted, and the third day, thin or thick soup. The fourth day a little zweiback is added, and by the fifth day the ordinary diet can be resumed.

Sodium Bicarbonate. Not much is heard today about giving sodium bicarbonate intravenously, which would indicate that this form of administering the drug, as usually performed, is either without benefit or actually harmful. To really determine the value of sodium bicarbonate given intravenously, the ordinary technic of sterilizing a solution of the drug by heat is faulty, inasmuch as the bicarbonate under these conditions changes to the carbonate, even if the temperature employed is considerably below the boiling point. It seems that such imperfect technic in the past may have actually led to bad results in some instances.

¹ Therap. Gazette, June, 1916. ² München. med. Wehnschr., January 11, 1916.

An interesting contribution to the subject of sodium bicarbonate *in surgery* has been made by Berkman¹ of the Mayo Clinic. In this clinic the use of sodium bicarbonate has become a routine for all patients with glycosuria who are subjected to operation, and it is the belief that this treatment has contributed in no small degree to the recovery of the patients. Dram doses by the mouth are given six to eight times daily, three or four days before the operation, and treatment is resumed as soon after operation as possible. When the surgeon finds it necessary to give rectal salines, soda is administered in this way also. Occasionally it has been found advisable to give it by intravenous injections in 5 per cent. solutions. During the postoperative observation, the urine is watched carefully, although keeping it free from sugar is more difficult, and is not as important as before operation. Twenty-six glycosuric patients came to operation. Two patients died, a mortality of 7.7 per cent. Eight patients were passing less than 10 gm. of sugar in twenty-four hours on an ordinary diet; and, other conditions being satisfactory, they required very little postoperative treatment, and that largely for the purpose of observation.

SODIUM BICARBONATE IN ACIDOSIS OF VARYING ETIOLOGY IN INFANTS AND OLDER CHILDREN. Acidosis is not an uncommon condition in infancy and childhood, according to Howland and McKim.² While it appears with special frequency in the severe diarrheas of infancy, it may occur in a variety of diseases, and sometimes, apparently, alone. To recognize it with older children is not very difficult. The hyperpnea is usually sufficient to arrest one's attention, and one or two relatively simple laboratory tests will quickly determine the question one way or the other. With infants who are irritable, restless and crying, it is much more difficult to say whether hyperpnea is present; and yet with them it is most important to make the diagnosis early, for the reason that acidosis is such a fatal complication of diarrheal disease in infancy. Older children react promptly and often permanently to alkali treatment. It may be possible to stop the clinical and laboratory evidences of acidosis in infants, but the patients usually die. Why they do cannot be determined at the present time. Many normal processes have undoubtedly been inhibited, perhaps permanently, and many abnormal ones stimulated. A restoration to normal conditions seems nearly impossible. For this reason we should not wait until acidosis can be demonstrated. From the beginning we should give bicarbonate of soda to infants with severe diarrhea in sufficient quantity to render the urine alkaline and keep it so.

The alkalis may be given by mouth, by rectum, subcutaneously, or intravenously. Vomiting and diarrhea frequently render their adminis-

¹ Journal-Lancet, June 1, 1916.

² Bulletin of the Johns Hopkins Hospital, March, 1916.

tration by mouth or by rectum out of the question. Then one of the other methods must be employed. Intravenous administration is the method of choice, especially when rapidity of action is desired—and with acidosis rapidity of action is always desired. The superior longitudinal sinus, as advised by Marfan, Tobler, and Helmholtz, is available with infants or the external jugular, or femoral veins. In older children, a vein in the arm can often be employed. If facilities for the intravenous injection of alkali are not at hand, the injection may be made subcutaneously with care that the bicarbonate has not been transformed into the carbonate, else severe sloughing of the tissues may result. A 4 per cent. solution is usually employed for intravenous use, and a 2 per cent. solution for subcutaneous use. The quantity to be used depends upon the size of the child, the severity of the symptoms, and the effect produced, but the amount is always large. It must be given till the urine becomes alkaline; even in infants under one year, as much as 10 gm. in twenty-four hours may be necessary. Water is urgently required, especially with infants who are depleted as a result of the vomiting and diarrhea. Under certain conditions, the administration of glucose is also indicated.

Tethelin. Robertson¹ has isolated a substance from the anterior lobe of the pituitary body which he considers to be the growth-controlling principle of this organ and has called it "tethelin." While tethelin may be regarded as being related to the physiologically active substances of the posterior lobe, relatively large doses are required to produce even a very slight transient fall in blood-pressure, and no diuresis is effected. The average yield of an anterior lobe of the pituitary body of an ox is about 10 mg. of tethelin. Administered in doses of 4 mg. per diem by mouth to mice between four and sixty weeks of age, tethelin causes a marked retardation of the early (preadolescent) growth in weight, an equally marked acceleration of postadolescent growth. Mice which have received tethelin are much more firmly and compactly built than normal animals of the same age. Weight for weight, the tethelin fed animals are smaller than normals, and size for size they are heavier. The favorable action on the nutrition of the skin is particularly marked.

Impressed by the stimulating effect on growth possessed by tethelin at least subsequently to adolescence, Robertson considered it very probable that it would also accelerate that species of internal growth which consists in the replacement of tissue lost through excessive tissue waste consequent on any circumstance leading to an increase in nitrogen output (for example fevers) or a curtailment of nitrogen intake (for example, inanition). With this thought in mind, he undertook two sets of experiments, the first, to determine the effect of tethelin in stimulating action on tissue repair, as expressed in the replacement of tissue lost

¹ Journal of the American Medical Association, 1916, lxvi, 1009.

during a preceding period of inanition, and second, to determine its effect in promoting the healing of granulating wounds. In both sets of experiments both male and female mice were employed. In the nutrition experiments the animals were starved and then abundantly fed, some being given hypodermic injections of 10 mg. of tethelin when feeding was resumed, the others being used as controls. The administration of the tethelin lead to a very remarkable acceleration of the regain in weight following admission to food after inanition in both sexes, the increase in weight being decidedly more gradual in the untreated mice. The stimulating effect persisted for at least thirty-six hours. Likewise in the case of the healing of experimentally produced wounds in the skin, granulation and cicatrization were strikingly accelerated in those mice that had received 10 mg. of tethelin hypodermically in contrast to the slower and more usual process of healing observed in the control animals. Certainly such lines of investigation deserve to be prosecuted to the utmost.

Transfusion. With improvements in technic and more extensive application, the transfusion of blood from a healthy person to a patient has become a well-recognized and valuable adjunct in therapy in certain conditions, and its limitations more clearly defined. How much the subject remains yet to be developed it is difficult to estimate. Clinical experience in the selection of cases for transfusion, and proper technic in its application, are essential to success. Several valuable papers dealing with transfusion have appeared during the past year or so, for example; that by Ottenberg and Libman¹ that by Peterson² that by Lewisohn,³ that of Satterlee and Hooper⁴ and articles in the *Journal of the American Medical Association* during June, 1916, under the heading of Therapeutics.

Modern methods have tended greatly to the elimination of the danger associated with transfusion and it is stated that there need be no fatal cases traceable to the transfusion itself, though great care and caution are essential to prevent disaster. Untoward symptoms or actual fatalities, when occurring as a result of the transfusion, may be traced to some disturbing element in the introduced blood; to the formation of a thrombus, to the introduction of an embolus, or to the dilation of an already weakened heart by too large an injection of blood, or by a too great pressure exerted in the introduction of the blood.

The symptoms arising as a result of transfusion may be trivial and temporary, others may assume a more serious nature. They may resemble the symptoms seen in serum sickness, with a rise in temperature, chills and the appearance of an urticarial rash. Others are of an anaphylactic nature and accompanied by shock.

¹ American Journal of the Medical Sciences, July, 1915.

² Journal of the American Medical Association, 1916, lxvi, 1291.

³ Ibid., December, 1915.

⁴ Ibid., 1916, lxvi, 618.

Agglutination and hemolyses of the patient's blood by the introduction of the blood from the donor can be avoided by proper preliminary tests, and the presence of syphilis in a possible donor can likewise be determined. The degree to which other disturbing elements may exist in the blood of the donor, and the special susceptibilities on the part of the patient's blood, need further investigation. Aseptic technic has greatly facilitated the operation of transfusion. Coagulation of the blood, which has in the past been a serious consideration, is a difficulty that seems to have been pretty well overcome. Among the anticoagulants that have been advocated, herudin (an extract from leech) and sodium citrate, the latter having proved to be the safer and more reliable. When sodium citrate is employed, the blood may be drawn from a donor into the citrate solution and carried to another place and even kept on ice for several days. Weil has advocated the use of the citrate at the ratio of 1 to 100 of blood, or 1 per cent. Lewisohn contends that sodium citrate may become toxic in these proportions if sufficient blood is transfused. Such proportions are not only capable of injury, but, according to Lewisohn, are unnecessary, a 0.2 per cent. strength answering clinical requirements; that is, 2 grams of sodium citrate to 1000 c.c. of blood.

Two general methods of transfusion are available—the direct and the indirect. In the direct method the artery or vein of the donor and the vein of the recipient are brought into connection by direct suturing, or by a tube or cannula. Various objections to these methods exist, such as complexity and the risk of clotting. In the indirect method the blood is withdrawn from the donor and then injected into the vein of the recipient. For this, Unger's apparatus has many advantages. It possesses a central stop-cock, being so arranged that the blood drawn out from the vein of the donor with a 20 c.c. syringe could be injected into the vein of the recipient with the same syringe. Needles or cannulas are inserted into the veins of both donor and recipient, as in the less satisfactory Linderman method, and these are connected with the apparatus. Only one syringe is required and at no time is the blood exposed to the air. An additional feature of the apparatus is that the passages traversed by the blood can be kept clean by flushing them occasionally with sterile saline solution by means of another syringe attachment. Very good results without secondary symptoms have been reported with Unger's apparatus.

The employment of an anticoagulant, preferably sodium citrate, in the indirect method has been strongly recommended. If it is as simple and safe in children as Lewisohn claims, it should certainly be a valuable method of transfusion in adults. Lewisohn with this method has been able to inject blood even in small children through a superficial arm vein of the finest caliber. He considers the fine needle used under these circumstances as valuable because it assures the slow injection of the blood, thus preventing the sudden overloading of the circulatory system. The donor's vein is punctured proximally or distally, the direction to be

chosen according to the individual case, whichever way the blood runs with the greatest facility into the glass receptacle. The blood is mixed in the glass jar with a 2 per cent. sterile solution of sodium citrate at the ratio of 1 to 10 (*i. e.*, 10 parts of solution to 100 parts of blood).

Some of the results of Ottenberg and Libman in transfusion for a variety of conditions are very briefly as follows:

1. Transfusion for *simple hemorrhage*. In duodenal or gastric ulcer the hemorrhage was stopped in 12 of 14 cases in which the conditions were desperate. Less success was encountered in dysentery, 4 out of 6 cases so treated dying of a continuation of the dysentery. In typhoid fever in which nine transfusions were performed in 7 cases, two of the patients ultimately recovered. The authors insist that "in all typhoid cases, the first appearance of blood in the stools should be an indication to make preparations so that transfusions can be done, if needed, at very short notice." In bleeding in ectopic pregnancy, transfusions was life-saving in all 3 cases transfused.

2. Transfusions done in connection with *surgical operations*. In 33 preoperative transfusions, 13 patients recovered from the operation. Some of the others died from postoperative complications. There were 3 brilliant recoveries in 5 transfusions for postoperative hemorrhage. In shock, however, transfusion proved disappointing.

3. Transfusions for the cure of *hemorrhagic conditions*. In 9 cases of purpura hemorrhagica, 6 recovered completely. In hemophilia, in out of 6 cases the hemorrhage ceased, and the patients regained good health. In hemorrhage secondary to infection, in one, a case of a newborn, the hemorrhages were checked. In another with gonorrheal rheumatism, transfusion was followed by recovery, but in a third case of hemorrhagic diphtheria, the patient died. In 3 cases of acute leukemia with hemorrhages, the hemorrhages did not cease after transfusion, whereas in one chronic case it did. In cases in which hemorrhages were combined with jaundice, the results were very disappointing.

4. Transfusion for *blood diseases*. In pernicious anemia, 35 transfusions were employed in 25 cases. In 14 cases there were more or less prolonged remissions, in none was a cure effected, and in 11 no effect was observed. In one case in which a splenectomy following three transfusions was performed, the patient returned to excellent health. In leukemia only the chronic cases showed any improvement in the blood picture, but even with these the effects were only temporary.

5. Transfusions for *infections*. Transfusion in infectious diseases was employed only as a last resort in some of the very desperate cases, 4 out of 10 so treated recovering. Three of these successful cases were osteomyelitic infections due to the staphylococcus. The fourth case was a streptococcal infection. In endocarditis, 3 out of 4 cases showed temporary improvement, but all eventually ended fatally.

6. Transfusions for *intoxications*. In cases of poisoning due to carbon

monoxid, hydrocyanic acid, benzene, or nitrobenzene, when these have acted on the blood to a marked degree, transfusion is of value, but a preliminary phlebotomy is very essential. Diabetic coma ended fatally in 4 cases transfused for this condition.

7. Transfusion for *debilitated conditions*. In debilitated conditions caused by cancer, transfusion without surgical interference is without result. The anemia of tuberculosis, however, is relieved by this treatment. In the simple anemias due to malnutrition or other minor causes, transfusion is justified, and satisfactory results can be obtained.

Lewisohn obtained excellent results with transfusion in all of seven children, four being hemorrhagic cases, one a case with extensive burns, and two were cases with severe anemia.

Vaccines. Reports from those who are employing vaccines continue to pour in from many sources. Whatever one's opinion may be as to the value of vaccines, it certainly is established that due caution should be observed in their employment, at least to the extent that no harm is occasioned. There is no question that their misuse has been attended with serious results. As Stengel¹ has pointed out, there is a wide difference between giving drugs by the mouth and giving vaccines subcutaneously or intravenously, for in the former case even toxic drugs in sublethal doses may be tolerated, or, if irritating, they may be rejected, safeguards that are wanting in subcutaneous and intravenous injections of vaccines or serums. A form of therapy so delicate and specific, and even in the most competent hands presenting so many phases that still remain obscure, should not, to say the least, be undertaken lightly. As a rule, it is considerably safer to give vaccines subcutaneously than intravenously. The administration of vaccines, according to McCabe, is usually attended with more risk than that of serums. The dosage and form of administration whether subcutaneous, intramuscular, subdural or intravenous will vary with the conditions.

The subject of the use of *commercial vaccines*, polyvalent and mixed, is one on which there still exists a seemingly irreconcilable difference of opinion, but such weighty influence is opposed to their routine use that without very good reason one should hesitate to resort to these forms of vaccines. Hektoen² concludes that the general results from the use of commercial vaccines so far have no value as evidence for or against the curative usefulness of vaccine treatment, and hence no value with respect to the soundness of the theory on which vaccine treatment primarily has been developed. Billings³ considers that vaccination, as practised all over the country by the use of commercial vaccines, is a disgrace to the medical profession. Fussell is greatly opposed to the present indiscriminate use of commercial vaccines and serums.

¹ Philadelphia County Medical Society, October 13, 1915.

² Journal of American Medical Association, 1916, lxi, 1591.

³ Transactions Association of American Physicians, May, 1916.

The importance of using *autogenous vaccines* when these are available continues to gather support from many, though by no means from all, sources. Rosenow¹ appears to have clearly demonstrated that organisms obtained from certain tissues possess the characteristics of having an affinity for similar tissues in other animals, or in human beings. Thus he found that 14 strains of streptococci from a case of appendicitis produced lesions in the appendix of 68 per cent. of the animals injected, while only 5 per cent. of the animals injected with strains of streptococci obtained from other sources than cases of appendicitis suffered from a localization of the organisms in this part of the body. Much the same results were obtained with the employment of streptococci obtained from the gall-bladder in cases of cholecystitis, and from the endocardium in cases of endocarditis, in producing cholecystitis and endocarditis in animals.

Hulst,² summarizing the literature, shows that at least some species of bacteria are able to acquire new characteristics, being unstable and able to change their metabolic processes to meet their environment. Variation occurs under the influence of weak chemical solution, salt concentration, oxygen tension, and symbiosis with other organisms so that it seems likely that similar changes may occur in the body in the course of infections where environment is also variable to the parasite. Examples of this kind have been encountered in cases in which streptococci obtained in puerperal sepsis may differ from those obtained from a metastatic abscess from the same case. Hulst states that "the selective action which organisms display toward certain tissues of the body may be acquired within the body to a certain extent. If these are alterations in the constitution of the parasite depending upon the conditions existing at the point of infection, this fact may determine the nature which the disease may assume as much as the parasite itself. Just what characteristics of bacteria control the affinities for various structures is not explained, but such affinities exist as well-marked phenomena, and bacteria undergoing experimental mutations show different affinities at different stages of their transformation."

From Rosenow's research, and the summary of Hulst, we find strong argument for the use of autogenous vaccines, because of the many strains of microorganisms belonging to the same family, and because of the changes to which bacteria are subject dependent upon the environment furnished by the individual who has become their host.

In subacute and chronic localized infections, Hektoen³ considers that specific vaccines properly and skilfully used have value, "quite likely because they increase the production of specific antibodies, as demanded by the theory, but probably also because they stimulate leukocytic and other activities." Hektoen believes that in typhoid fever and possibly

¹ Journal of the American Medical Association, November 13, 1915.

² Long Island Medical Journal, November, 1915.

³ Journal of the American Medical Association, May 20, 1916, p. 1592.

also in other infectious diseases, the intravenous injection of specific vaccines and also of other substances may induce crisis and prompt recovery. He admits that the mechanism of this action is not fully understood, and considers that we are entering a new and interesting development in the study and treatment of infectious diseases.

Billings's¹ experience with the use of autogenous vaccines in chronic processes, both local and general, had not been encouraging. He considers that their use is so limited that their employment has not justified the expenditure of labor and the price necessary to carry on the work. "That is a general statement, subject to modification that in certain instances, under certain conditions, and in certain individuals, the use of vaccines seem to be of benefit: but take them as a class in general disease, I have yet to see the benefit from them."

The value of *sensitized vaccines* is endorsed by Wohl.² He outlines the method of modifying sensitization of vaccines as carried out at the Nicholas Senn Hospital in Omaha. His results in a number of different conditions though rather few encourage the author to advocate their wide application. He concludes: (1) Sensitized vaccines are superior to unsensitized. (2) The use of the patient's own serum for sensitization is scientifically justified. (3) The use of the serum and sensitized vaccines is based upon scientific data, and clinically is proving of great value.

COMBINED VACCINATIONS. Castellani, in 1901-2, in Professor Kruse's Institute, demonstrated that inoculating an animal with three species of bacteria, provided a sufficient minimum quantity was given, agglutinins and immune bodies for all three species were elaborated, the amount of agglutinins and immune bodies elaborated for each being nearly the same as in animals respectively inoculated with one species only. In the *Indian Medical Gazette*, November 1915, he states that with rabbits he has not as a rule obtained good results by inoculating more than three species of bacteria. In man it appears that four species can be inoculated with satisfactory results, and occasionally even more. Castellani has prepared and used in man eleven different combinations, made up of two or more of the following vaccines: typhoid, paratyphoid A, paratyphoid B, Malta fever, b. asiaticus, b. columbiensis, dysentery Kruse-Shiga, dysentery Flexner, dysentery Hys. V., dysentery Flexner-like No. 1, dysentery Flexner-like No. 2, cholera and plague. The inoculations in man of the combinations he has employed have proven harmless in his hands. The reactions have not been very severe except with two of the combinations.

The individuals inoculated with these combined vaccines, consisting of two, three and four species of bacteria, generally produce agglutinins for each species of bacteria inoculated, and the amount is not much less

¹ Journal of the American Medical Association, vol. lxvi, p. 1741.

² American Journal of the Medical Sciences, August, 1916.

than in control individuals inoculated with simple one-disease vaccines. As regards vaccines consisting of more than four species some seem to induce production of a fair amount of agglutinins for all the species, others do not give such satisfactory results, agglutinin developing only for certain species and not for all. The combined vaccines which Castellani has found most useful from a practical point of view are the "typhoid and paratyphoid A and paratyphoid B" prepared and used by him since 1905; the "cholera and plague vaccine" the "typhoid and paratyphoid A and paratyphoid B and Malta fever," and the "typhoid + paratyphoid A + paratyphoid B + cholera." Castellani contends that the use of efficient mixed vaccines is of practical advantage, as it is in this way possible to give a certain degree of contemporaneous immunity for several different maladies. This procedure saves a great deal of time and trouble. Moreover, in his experience, very few people will submit themselves to the discomfort of repeated injections, which would extend over a period of several weeks in order to be inoculated against three or four different diseases. This subject will be referred to later in speaking of typhoid fever.

ASTHMA. Any form of treatment which holds out hope of benefit in cases of asthma that do not yield satisfactorily to the ordinary lines of treatment is to be encouraged. Royers¹ claims to have obtained promising results in a number of cases of this disease, taking cultures directly from the sputum. Klink² claims also to have had gratifying results with autogenous vaccines in the treatment of 12 or 15 cases of asthma.

GONORRHEA. Renewed interest in the vaccine treatment of gonorrhea may be expected from the favorable reports of the use of *gonococcus fats* as advocated by Warden.³ Warden states that the fats of the gonococcus, chemically isolated from the organism and suspended in alcohol, possess a much higher antigenic power than the watery antigens of commerce. The cases treated comprised acute, chronic, simple and complicated, cases of gonorrhea, on men and infant girls. In all, the subcutaneous inoculation of the fats is reported to have been followed by marked improvement, and in some by undoubted cure.

PNEUMONIA. The efficacy of serum treatment in Type I infection in pneumonia as advocated by Cole is substantiated by the experience of Park in New York City, who states that up to the present time the mortality has been much less in the treated than in the untreated cases. Park encountered serum sickness in about 50 per cent. of the cases, which, though annoying, did not prove dangerous. He believes that in severe cases a first dose of Type I serum should be given as soon as possible and the later injections only after a bacteriologic report has been received.

¹ Practitioner, June, 1916.

² Missouri State Medical Association, May, 1916.

³ Journal of the American Medical Association, December 11, 1915, p. 2089.

PUERPERAL FEVER. Two cases of puerperal fever caused by streptococci are reported by Chalmers and O. Farrell¹ to have been successfully treated with autogenous vaccines. The first case was cured following the use of an autogenous vaccine, after preliminary failure with the employment anti-streptococcal serum and a stock vaccine.

TYPHOID FEVER. Antityphoid vaccinations to the number of 8124 are reported for California by Sawyer.² True failures occurred in 5.0 per thousand vaccinations reported, and the deaths from typhoid fever were 0.49 per thousand. The percentage of failures indicated a slight advantage for the Gay-Claypole sensitized vaccine over the unsensitized vaccines, but the superiority was not conclusively demonstrated as the different sets of statistics were not exactly comparable.

Besides Castellani, whose work has already received reference, a number of others,³ Kabeshima in the Japanese Navy, Vincent, Widal, Chantemesse, and Dreyer, furnish evidence in favor of the use of mixed antityphoid and antiparatyphoid inoculation. The convenience of the method speaks for itself, and the practical value of the simultaneous use of these vaccines seems to be quite as great if not greater than successive inoculations with the different vaccines.

The reaction to antityphoid vaccination has been carefully studied by Tonnell⁴ in 30 healthy soldiers and in 20 who were already under hospital care. He found constantly more or less of a reaction in the blood and urine, the reaction in some of the men being actually pathologic. Strangely, the reaction was least intense in the tuberculous and those with albuminuria, while some of the apparently healthy responded with a pathologic reaction. More or less destruction of red corpuscles was encountered, a loss of half a million being an average. A loss of toxicity of the urine to infusoria was noticed after the vaccinations.

The treatment of typhoid fever with vaccines still seems to be in a formative stage, the best results apparently being largely restricted to a shortening of the duration of the disease. Gay and Chickering⁵ report on 75 cases of typhoid, the majority being treated with intravenous injections of polyvalent, sensitized vaccine sediment. The mortality was about 9 to 10 per cent. Distinct benefit was seen in cutting short the disease. A mortality of 14 per cent. was experienced by Wiltshire and MacGillycuddy⁶ using stock vaccines. Whittington⁷ treated 115 cases of

¹ Journal of Tropical Medicine and Hygiene, London, April 1, 1916.

² Journal of the American Medical Association, October 23, 1915, lxx, 1414.

³ Editorial, Journal of the American Medical Association, January 15, 1916, lxxi, 193.

⁴ Lyon Médical, Lyons, April, 1916.

⁵ Transactions Association of American Physicians, Meeting held at Washington, May, 1916.

⁶ London Lancet, September 25, 1915.

⁷ Ibid., April 8, 1916.

typhoid with stock vaccines and used 115 others as controls. The mortality among the inoculated cases was 25 per cent., among the controls 20 per cent. Whittington does not recommend the routine use of stock vaccines in treating typhoid fever. McWilliams¹ reviewing over 550 cases of typhoid from the literature, states that in more than one-half the disease was cut short, the patient having been saved from one to several weeks of fever. McWilliams believes that a few deaths must undoubtedly be attributed directly to the injections of vaccine, but he encouragingly remarks that this is likely to occur with any new and radical method of treatment.

Vaccine therapy depends so much for its successful development upon the knowledge gained in the production of artificial immunity against various infectious diseases that a few references to the excellent paper on Immunization and its Practical Applications delivered by Theobald Smith² before the Association of American Physicians in May, 1916, will be timely. Smith gives two underlying principles of immunization: "(1) To prevent or check disease by applying the methods copied from nature and improving on them in the interest of man, if possible. (2) To discover the *modus operandi* of resistance to disease, the sequence of events which is associated with recovery on the one hand, and with complete resistance on the other. The object of immunization is to raise the resistance of the body." "We must accept the fact that no kind of vaccination is invariably and completely protective. We may, however, hope to convert a fatal into a non-fatal attack, a mild attack into one so mild as to remain unrecognized, or into complete protection."

"Our present conception of acquired immunity assumes that after every exposure there is some, however slight, multiplication of the virus necessary to wake up the immunizing mechanism." "The essential factor to be kept in mind is to raise such resistance with the least injury to the subject. The direction which immunization is to take depends on the etiologic factors involved. There are primary and secondary infectious agents in most diseases." "The question, then, at issue becomes a choice of vaccine toward possible secondary invaders. The general rule that a single attack of a disease protects for life is subject to many limitations. All acquired immunity is a perishable commodity. This question is complicated by several factors, among which are the following: (a) The human body becomes more resistant to infection with age. (b) There is a possibility of reinfection without clinical signs which will maintain and strengthen any immunity obtained in infancy and childhood." "Among the established facts in immunology is the greater efficacy of living virus over any other; the practical application of this fact, however, encounters many obstacles." "Next to living virus the

¹ Medical Record, New York, October 16, 1915.

² Journal of the American Medical Association, May 27, 1916, p. 1740.

bodies of bacteria killed by heat seem to have the best chance of producing immunity. The success or failure of this method will depend theoretically on what is the most important antigen." "The relative efficiency of sensitized vaccines probably depends on a quantitative relationship between the antiserum and the bacilli." "The explanation for the very effective immunizing power of sensitized toxins depends on the greater penetrating power of such mixtures."

Venesection. Venesection continues to be a valuable method of treatment in properly selected cases, according to the opinion of many clinicians, though as a rule they do not use it under more than a limited number of conditions. Lawrence¹ believes that in the presence of dilatation of the heart, renal toxemia, hypertension, or a combination of these conditions, venesection may be expected to act more promptly and more surely than drugs. In cases of hypertension it lowers blood-pressure and at the same time produces a more efficient circulation, though it does not in normal arterial tension, lower the blood-pressure in "therapeutic doses." While venesection should only be employed in the presence of definite indications, it should not be withheld until hope of success from any measure is gone. The amount of blood to be withdrawn is to be decided by the point at which relief is obtained. The error is generally on the side of too small an amount. Repeated blood letting, when indicated, does not seem to have any ill effects on the composition of the blood.

In some instances, however, there seems to be an enlargement of the sphere in which blood-letting is recommended. In women at the menopause in whom there is high blood-pressure in association with certain cardiovascular disturbance, Engelhoon² has derived benefit from this treatment. The annoying "hot flashes" with the usual sensation of heat and attacks of sweating and redness all subsided. He believes the effects produced were not psychical in nature, as the patients were not informed of the purposes of the venesection, though it seems difficult to exclude the psychical factor altogether. In analogous nervous phenomena sometimes occurring at puberty, and attributed to a deficit or perversion in ovarian functioning, manifested by amenorrhea, dysmenorrhea, infantilism, chlorosis and other disturbances, Engelhoon has witnessed gratifying results with venesection. He only withdraws small quantities of blood, not over 100 c.c. at a time, though he has repeated the blood-letting in a few cases.

Theilhaber³ has employed venesection 450 times in the last eight years. He is particularly enthusiastic about its value in the hot flashes of the menopause, being invariably beneficial and never harmful. Some patients with dysmenorrhea were relieved by the treatment, inter-

¹ Boston Medical and Surgical Journal, February 24, 1916.

² München. med. Wehnschr., November 9, 1915.

³ Berl. klin. Wehnschr., November 22, 1915.

menstrual colic sometimes yielded to venesection. Neuralgia and the neurosis, especially nervous headaches in the plethoric, were benefited. Another indication for venesection is an adjuvant to diathermia in prophylaxis of recurrence after operations for cancer. He gives periodical blood-lettings under these conditions to stimulate the blood-producing organs, usually twice a year withdrawing 400 to 500 c.c. at a time. He refers to Jichera's experiments on animals that tend to show that periodical venesections enhance the resisting power against inoculation with cancer. Theillhaber believes that cancer develops by preference in anemic tissues, and that the slight transient anemia from venesection is soon followed by a wave of greater production of blood.

X-rays. THE X-RAY IN THE TREATMENT OF PULMONARY TUBERCULOSIS. Sceptical as one may be of any of the known special methods of treating pulmonary tuberculosis, it is proper to encourage every line of work that offers any promise and is still imperfectly developed. Such in a general way may be considered the röntgen treatment of tuberculosis of the lungs at the present time. An optimistic view of this line of treatment is held by Kupperle and Baemeister¹ who report remarkable success in the treatment of rabbits inoculated with tubercle bacilli and systematically exposed to the rays, larger doses and shorter intervals than those previously employed being used. The tuberculous process was considered to have been healed over, but the tubercle bacilli themselves were not killed. The results were considered sufficiently promising to warrant the application of the treatment to human beings. Hard, filtered rays were used and 20 cases of stationary pulmonary tuberculosis, without fever, and with a tendency to latency, are reported who received the treatment, and also a number of fibrile and chronically progressive cases. The course was considered as completed by 10 patients in this latter group, and all were reported as clinically cured. In every case improvement was manifest.

The authors consider that the experimental and clinical data all indicate that the Röntgen rays act only on the relatively rapidly growing tuberculous granulation tissue. Extremely virulent and rapidly destructive processes are not influenced by them, nor are caseous processes or the tubercle bacilli themselves.

The value of the x-ray in the treatment of *enlargement of the thymus* gland is discussed by Grossman² who states that röntgen irradiation has been employed with favorable results in a number of cases. Flügge, Waters, Rudberg, Ambertin and Bordet, Sinorzersky, Myers, Lange, have demonstrated that thymic asthma and marked atrophy of the gland followed röntgenization, together with improvement in the symptoms. Involution begins in from one or two hours after exposure and

¹ Deutsch. med. Wchnschr., January 27, 1916.

² New York Medical Journal, November 27, 1915.

continues for a variable length of time according to the intensity of irradiation, regenerative changes gradually taking place after treatment has been discontinued. Caution is advocated in the employment of this treatment, as it may inhibit further growth in the tissues (proved by experiments on young animals) and also produce intoxication from the products of lymphoid disintegration.

In gynecological cases, the *x*-ray, like radium, is being constantly tested out. Thus favorable results in *uterine hemorrhage* are reported by Corscaden¹ who employed this form of treatment in twenty women, thirty-eight years of age and over, whether possessing fibroids or not. Complete amenorrhea was affected in 5 per cent. of cases from the onset of treatment, in 5 per cent. after one period, in 5 per cent. after three periods, and in 85 per cent. after two periods. The first period was occasionally found to be profuse. All of the cases were found to be severe enough to partially or completely incapacitate the women. Untoward effects were observed in only 2 cases, one suffering from nausea and diarrhea, the other from diarrhea indistinguishable from mucous colitis. No late effects other than those accompanying the menopause were noted except in 1 case in which there was an attack of uremia six months after the end of treatment in a woman suffering from large polycystic kidneys. Corscaden says that menstruation is dependent on the activities of the corpus luteum, and that the Röntgen rays destroy the follicle apparatus of the ovary, thereby automatically bringing about a menopause. All patients with myomas which do not constitute an immediate or remote menace aside from that of hemorrhage are proper subjects for the production of the menopause, provided that ulcerative changes or pedunculated fibroids or polyps do not exist, and provided that the possessor be over thirty-seven years of age. All myomas which constitute a menace in women under thirty-eight should be excised rather than subjected to Röntgen rays, unless operation is contra-indicated. In hemorrhage from malignant disease the rays are said to be contra-indicated.

Less favorable comments on this form of treatment in *uterine fibroids* are made by the October number of *American Medicine*, in which, while the value of *x*-rays in certain cases is not denied, the stand is taken that it should not be used save only when all other medical procedures, among which the administration of radium and mammary extract are given, have failed, which does not seem to have been done in most of the cases reported.

In discussing the Röntgen-ray treatment of *skin diseases*, MacKee² deplors the tendency to separate dermatology from röntgenotherapy. To avoid errors in diagnosis and the obvious consequences, it is suggested that one of three schemes be adhered to: for the dermatologist to employ

¹ American Journal of Obstetric and Diseases of Women and Children, January, 1916.

² Journal of the American Medical Association, 1915, lxx, p. 1886.

the Röntgen ray; for the röntgenologist to have at least a clinical knowledge of dermatology; or for both to combine their skill in behalf of the patient. In this paper the technic of treating skin diseases with *x*-rays is briefly outlined, and a number of affections discussed that are amenable to this form of therapy. Among these are erythema induratum, granuloma annulare, lichen planus, psoriasis, eczema, lichenification and lichen circumscriptus, pompholyx, calvus, callositas and verrucae, keloid, nevus vasculosus, rhinoscleroma, tuberculosis cutis, lupus erythematosus and epithelioma including Paget's disease.

Acne has now been subjected to treatment with *x*-rays during a sufficiently long time for the indications and contra-indications to be fairly well established. Dosseker's¹ experience, based on a large number of cases indicates that repeated small doses of the rays, not strong enough to induce appreciable reaction of the skin, or a single large dose with a reaction, seem to be able to modify the epidermis, that is, the sebaceous glands to such an extent that the tendency to acne dies out. The efficacy of this form of treatment is said to be greater in acne spread over a larger surface, with numerous pustules, than in the less disfiguring, torpid type.

Genereal buboes have been subjected to *x*-ray treatment by Kall² for eighteen months, as a result of the encouraging effects encountered in röntgenotherapy of tuberculous gland disease. The results have been so good that he urgently advocates this method in their systematic treatment, especially in the early stages before much inflammation has developed. The treatment is more successful before there is suppuration; the pain subsides and the patient is able to go about without disturbances of any sort from this source. Even after suppuration has set in, the leukocytes are destroyed by the Röntgen rays and all are apparently absorbed. The fluctuation, the pain and the redness all disappear, and the infiltration gradually retrogresses, but the spot is left pigmented. Even indolent syphilitic buboes are said to respond promptly to the Röntgen ray. Developed abscesses have to be evacuated with an incision, but the secretion ceases and the abscess heals quicker under subsequent exposures to the *x*-ray.

Yeast. Yeast is strongly urged by Willcox³ in the prophylaxis and treatment of *beriberi* on account of its content of anti-beriberi vitamins. It may be used in a variety of forms in which yeast is ordinarily procurable, such as the "export yeast" used in the present campaign, the "Royal yeast cakes" and in the form of yeast brew obtainable at the army bakeries. Extracts of yeast are on the market, and taste exactly like extract of meat, and when mixed with warm water form a drink like ordinary meat extract or bovril. Yeast extracts may be given with advantage in both acute and chronic beriberi cases.

¹ *Therapeutische Monatshefte*, August, 1915.

² *Münch. med. Wchnschr.*, October 19, 1915.

³ *London Lancet*, March 11, 1916.

INDEX.

A

ABDERHALDEN reaction in gastric ulcer, 51
 Abdominal disease, 83
 fremitus as a sign of chronic peritonitis, 83
 Abortion, pituitary gland in, 429
 Abscess, perinephritic, 191
 Accident surgery, 244
 Acetate of lead, 409
 Acetylsalicylic acid, 440
 Achylia gastrica, 68
 Acid, acetylsalicylic, 440
 boric, 385
 Acidity, gastric, effect of bile on, 76
 relations of splanchnoptosis to, 58
 shall it be estimated in filtered or unfiltered gastric contents, 76
 test for, without stomach-tube, 77
 in stomach and intestine, mechanism of neutralizing, 75
 of undiluted gastric juice, 75
 Acidosis in children, sodium bicarbonate in, 443
 in renal disease, 159
 Adenocarcinoma, primary, of kidney, 193
 Adrenalectomy and gastric ulcer, 40
 Adrenalin, 369
 Air in wound treatment, 254
 Albumin test for gastric ulcer, 47
 Albuminuria, orthostatic, phthalein test in, 142
 Alcohol injections in painful neuritis, 295
 Alcoholism, chronic, dyspepsia and, 63
 Allen treatment of diabetes, 395
 Ambard and Weill's coefficient of urea excretion, 152
 American first-aid conference, 244
 Aminolytic ferment in gastric contents in carcinoma, 50
 Amylase in pancreatic disease, diagnostic value of, 135
 Anesthesia, 242
 blood-urea findings before and after, 152
 intratracheal ether, 242
 Anesthetic, ethyl chloride as, 243
 infiltration, continuous stream syringe apparatus, 244
 Antidiphtheritic serum, 370

Antimetastatic serum in gonorrheal ureteropyelitis, 187
 Antimony, 378
 Antiseptics in wound treatment, 252
 Antitetanic serum, 372
 Antitoxic sera, 370
 Aortic insufficiency, digitalis in, 398
 Appendicitis, 111
 Blumberg's sign of, 111
 new sign of, 111
 Arbutin, 378
 Arrhythmia, digitalis in, 398
 Arsenic, 378
 Arteriosclerosis of abdominal vessels, 83
 Arthritis, rheumatoid, diet in, 391
 Artificial respiration, 378
 Ascites, chylous, 83
 Asphyxia, traumatic, 238
 Aspirin, 440
 Asthma, bronchial, pituitary gland in, 429
 vaccines in, 451
 Atropine, 379
 in gastric disorders, 382
 Autogenous vaccines, 449

B

BACILLUS, gas, in amputated stump, 279
 Bacteriology, surgical, 272
 Benign proliferation of glands in stomach, 54
 Benzol, 382
 Beriberi, yeast in, 457
 Bile, clinical studies of, 122
 effect of, on gastric acidity, 76
 in liver disease, microscopic study of, 123
 pigment, extra hepatic formation of, 120
 metabolism, 119
 reaction of, 119
 secretion of, 120
 Bismuth, 383
 Bitter tonics, 383
 Bladder, 179
 foreign bodies in, 195
 Blastomycetic dermatitis, 302
 Blood, alterations in composition of, 147
 non-protein nitrogen of, 147
 occult, 112
 tests for, 113
 with gastric cancer, 112
 pressure, 233

- Blood pressure, high, digitalis in, 398
 normal, 236
 in relation to kidneys, 147
 serum, 384
 transfusion, 385, 445
- Blood-urea findings before and after anesthesia, 152
- Blumberg's sign of appendicitis, 111
- Bone aneurism, 362
 cysts, 325
 in congenital fracture, 334
 of metacarpus, 336
 multiple, 331
 and osteitis fibrosa, 324
 subperiosteal resection of, 332
 of upper end of femur, 335
 graft, 325
 hemangioma of, multiple, 340
 sarcoma of, 333
 transplantation, 365
 tumors of, metastatic, 358
 thyroid, 361
- Bones, 322
 exostoses of, 322
- Boric acid, 385
- Bridge for gap in nerve suture, 289
- Buboes, venereal, x-rays in, 457

C

- CALCULI, pancreatic, 136
 renal, 179
 ureteral, 179
- Cancer of uterus, radium in, 437
 gastric, 40
 Abderhalden reaction in, 51
 albumin test for, 47
 aminolytic ferment in gastric contents in, 50
 digestion leukocytosis in, 52
 gastric ulcer and, 53
 differentiation of, 53
 laboratory tests for, 47
 miostagmin reaction for, 49
 occult blood with, 112
 oxyproteic acid test in, 52
 tumor autolysates in treatment of, 52
 urine color test for, 52
 x-ray diagnosis of, 41
- Cannabis indica intoxication, 386
- Carbohydrate factor in causation and treatment of hyperacidity and gastric ulcer, 28
 indigestion, 114
- Carcinoma of duodenum, clinical forms of, 96
 etiology of, 90
 evolution of, 95
 pathologic anatomy of, 92
 physical signs of, 94
 primary, 90
 symptoms of, 93
 of gall-bladder, 127
 of liver, 132
 of urethra, primary, 223
- Cardiospasm, 20

- Carrel's method of wound treatment, 256
- Chancroid, 221
- Chemism of stomach with duodenal ulcer, 88
- Chemistry, gastric, retention tube in study of, 75
- Chenopodium, 387
- Childhood, salicylates in, 439
- Chloride excretory function, 156
- Chlorine gas poisoning, 387
- Cholecystectomy, recurrence of gall-stones after, 126
- Cholelithiasis, treatment of, 124
- Cholesterol in food, is biliary cholesterol excretion influenced by, 121
- Chorea, magnesium sulphate in, 411
- Chylous ascites, 83
- Colon bacillus infection, chronic, lavage of renal pelvis in, 186
 movements of, 96
- Concrement in stomach, 72
- Corpus luteum, 388
- Cyanocupral, 388
- Cysts, bone, in congenital fracture, 334
 and osteitis fibrosa, 324
 of metacarpus, 336
 multiple, 331
 subperiosteal resection of, 332
 transplantation of fat in, 327
 of upper end of femur, 335
 osteitis fibrosa without, 325
 of posterior urethra, 225
 of prostate, 206

D

- DAKIN's solution in wound treatment, 254
- Dangers of oxygen injections, 277
- Death, cause of, in experimental pancreatitis, 135
 thymus, 241
- Decapsulation of kidney, 191
- Delirium tremens, magnesium sulphate in, 412
- Dental disease, relation between diet and, 393
- Dermatitis, blastomycetic, 302
- Diabetes, Allen treatment of, 395
- Diarrhea, gastrogenous, 116
 silver nitrate in, 442
- Diathermy in treatment of malignant vesical tumors, 197
- Diet, 390
 in chronic disease of intestine, 118
 heart disease, 390
 in gastric diseases, 391
 relation between, and dental disease, 393
 in rheumatoid arthritis, 391
- Digestion leukocytosis in gastric ulcer, 52
- Digitalis, 396
 in auricular fibrillation, 397
- Diseases, abdominal, 83
 of esophagus, 17
 of gall-bladder, 119
 of intestine, 83

- Diseases of kidney, 137
 of liver, 119
 of mouth, 17
 of pancreas, 133
 of stomach, 23
- Diuresis, 137
 cause of, excited by caffeine, 138
- Does cholesterol in food influence biliary cholesterol excretion, 121
- Drainage of wounds, salt sacks for, 260
- Duodenal contents, 88
 regurgitation of, into stomach, 89
 feeding, 89
 tube in gall-bladder disease, 122
 ulcer, 23, 83
- Duodenum, carcinoma of, 90
- Dysentery, magnesium sulphate in, 412
- Dyspepsia and chronic alcoholism, 63
 umbilical, 72
- E**
- ELECTRIC shock, 237
- Emboli, fat, 241
- Emetine, 398
 in amebic dysentery, 400
 during pregnancy, 400
- Enteroliths, 117
- Ergot, 401
- Erysipelas, 282
- Esophageal conditions, value of x-ray in diagnosing, 22
- Esophagus, diseases of, 17
- Ether anesthesia, intratracheal, 242
- Ethyl chloride as anesthetic, 243
- Excision and primary suture of wounds, 261
- Exercise, 402
- Exfoliative gastritis, 61
- Exostoses, 322
- Extract, leukocytic, 406
- F**
- FASCIA, 296
- Fat emboli, 241
 transplantation of, in bone cysts, 327
- Feeding, duodenal, 90
 rectal, 118
- Femur, bone cysts of upper end of, 335
- Fibrillation, auricular, digitalis in, 397
- Fibroids, uterine, x-rays in, 456
- Fibromyoma of prepuce, 222
- First-aid, 246
 conference, American, 244
 on firing line, 249
- Fixation in nerve injury, 284
- Flatulence and shock, 239
- Food problem in dispensary patients, 393
- Foot, perforating ulcer of, 300
- Foreign bodies in bladder, 195
 location of, in wounds, 261
 in wounds, 273
- Fractional method of examining gastric secretion, 74
- Fractures, gunshot, 268
 operative treatment of, 271
 x-rays in, 270
- Fuchsin, 104
- G**
- GALACTOSE test for liver function, 128
- Gall-bladder, carcinoma of, 127
 diseases of, 119
 duodenal tube in, 122
 movements of, 119
- Gall-stones, recurrence of, after cholecystectomy, 126
- Gangrene, gas, inflammability of gas in, 278
- Gas bacillus in amputated stump, 279
 quinine as specific for, 276
- gangrene, inflammability of gas in, 278
 phlegmons, 275
 x-ray in, 280
- Gastric acidity, effect of bile on, 76
 shall it be estimated in filtered or unfiltered gastric contents? 76
 test for, without stomach-tube, 77
 cancer, 40
 chemistry, retention tube in study of, 75
 diseases, diet in, 391
 juice, acidity of undiluted, 75
 motility, 64
 residuum in normal individuals, 78
 secretion, fractional method of examining, 74
 ulcer, 23
 and cancer, 53
 carbohydrate factor in treatment of, 28
 vertigo, 71
- Gastrin, 80
- Gastritis, 60
 exfoliative, 61
 typhoid, 60
- Gastrojejunal ulcers, 53
- Gastrogenous diarrhea, 116
- Gastroptosis, 55
- Giant-cell tumors of bone, 342
 multiple, 355
- Glands of stomach, benign proliferation of, 54
- Gonorrhea, vaccines in, 451
- Gonorrheal ureteropyelitis treated by antimeningococcic serum, 187
- Granulating wounds, 262
- Gunshot fractures, 268
 wounds, 250
 of joints, 263
 bacteriological control of, 265
 first treatment of, 263
 hyperemia in, 265
 position for ankylosed joints after, 267
 resection after, 267

H

- HAND, tendons of, infection of, 313
wounds of, 263
- Hay fever, pollen toxin in treatment of, 431
- Heart diseases, chronic, diet in, 390
massage in shock, 240
right-sided hypertension of, a post-operative complication, 240
- Heliotherapy, 405
in treatment of lupus, 406
of skin diseases, 406
of wounds, 405
- Hemangioma of bone, multiple, 340
- Hematoma, muscle, 305
- Hemoglobinuria, malarial, quinine in, 435
- Hemorrhage, secondary, in wounds, 262
uterine, x-rays in, 456
- Hemorrhagic cystic sarcoma, 362
- Hepatic disease, urinary findings in, 130
- Hexamethylenamine, 407
- High-frequency current in urethral lesions, 224
- Hospital, base, unit plan for, 250
- Hüter's sign, 307
- Hydrochloric acid, free, paper test for, 78
- Hyperacidity and duodenal ulcer, 86
- Hypernephroma, 193
- Hyperthyroidism, quinine in, 436
- Hypophosphites, 407
in pulmonary tuberculosis, 407

I

- IDIOPATHIC megacecum, 108
- Indigestion, carbohydrate, 114
- Industrial physicians and surgeons, 245
- Infection, 272
renal, lymphatic, ascending, 188
of seminal vesicles, 209
- Inflammability of gas in gas gangrene, 278
- Injury of nerves, 284
- Intestinal digestion after excision of large portion of small intestine, 110
obstruction, 109
non-coagulable blood nitrogen in, 109
proteose intoxication in, 109
stasis, 101
- Intestine, chronic disease of, diet in, 118
- Intestines, motor functions of, 99
- Intraneural injections for diagnosis and treatment of nerve injuries, 287
- Intrapericardial injections of epinephrin in shock, 240
- Intraspinal injections of bichloride of mercury, 416
- Intravenous administration of mercury, 415
gelatin solution in shock, 240
- Irrigation in wound treatment, 259

J

- JAUNDICE, obstructive, 132

K

- KAOLIN, 408
- Kidneys, 179
blood in relation to, 147
decapsulation, 191
diseases of, 137
function tests of, 141
pathological histology of, 139
primary adenocarcinoma of, 193
relation of, to blood-sugar, 138
rupture of, 189
tuberculosis of, 192
tumors of, 193

L

- LABOR, pituitary gland in, 430
- Laboratory tests for gastric ulcer, 47
- Lactic acid bacillus, 409
- Lavage of renal pelvis in chronic colon bacillus infection, 186
- Lead acetate, 409
- Lecithin, 410
- Leukocytic extract, 406
- Leukocytosis, digestion, in gastric ulcer, 52
- Liver, carcinoma of, primary, 132
diseases of, 119
microscopic study of bile in, 123
residual nitrogen in, 129
function, galactose test for, 128
phenoltetrachlorophthalein test for, 128
- Luetic myositis, 309
- Luetin reaction, effect of potassium iodide on, 432
- Lumbar puncture in nervous shock, importance of, 239
- Lupus, heliotherapy in, 406
- Lymph lavage in wound treatment, 260
- Lymphatic renal infection, ascending, 188

M

- MAGNESIUM sulphate, 410
in chorea, 411
in delirium tremens, 412
in dysentery, 412
in tetanus, 411
- Megacecum, idiopathic, 108
- Menorrhagia, pituitary gland in, 430
- Menthol, 413
- Mercury, 413
bichloride of, intraspinal injections of, 416
intravenous administration of, 415
in malaria, 417
poisoning, 413
- Mesothorium in treatment of malignant vesical tumors, 197
- Metacarpus, bone cyst of, 335
- Metastatic prostatitis, 208
tumors of bone, 358
- Metrorrhagia, pituitary gland in, 430
- Microscopic study of bile in liver disease, 123

Military orthopedics, 268
 surgery, 248
 Milk, pasteurization of, 394
 Miostagmin reaction in gastric ulcer, 49
 Morphine in shock, 240
 Motility, gastric, 64
 Motor functions of intestines, 99
 Mouth, diseases of, 17
 Movements of colon, 96
 of empty stomach in pathological
 states, 73
 of gall-bladder, 119
 Multiple bone cysts, 331
 Muscle hematoma, 305
 rupture, 306
 Hüter's sign of, 307
 Muscles, 304
 Myalgia, 308
 Myoma of stomach, 72
 Myositis, luetic, 309
 ossifying, 309

N

NATIONAL committee on medical and
 surgical preparedness, 248
 research council, 248
 Nephritis, 163
 treatment of, 165
 trench, 175
 Nerve concussion, 284
 fixation in, 284
 grafting and implantation, 289
 injuries, painful, operations for, 293
 suture, bridge for gap in, 289
 Nerves, 284
 gross pathology of, 292
 injury of, 284
 conclusions on, 295
 exploratory operation in, 288
 indications for operation in, 286
 operative methods in, 288
 time to operate in, 286
 ultimate results of, 293
 microscopic pathology of, 292
 Nervous furring of tongue, 19
 Neuralgia in vesical and prostatic disease,
 treatment of, 204
 Neurasthenia gastrica, 69
 Neuritis, painful, alcohol injections in, 295
 saline injections in, 442
 Neurolysis, 293
 Neuroses, war, 229
 New growths of prostatic urethra in rela-
 tion to tuberculosis, 226
 Non-coagulable blood nitrogen in intes-
 tinal obstruction, 109
 Non-protein nitrogen of blood, 147

O

OBSTETRIC practice, pituitary gland in,
 429
 Obstruction of ductus choledochus, press-
 ure of bile during, 133
 intestinal, 109

Obstruction, intestinal, non-coagulable
 blood nitrogen in, 109
 proteose intoxication in, 110
 Obstructive jaundice, 132
 Occult blood, 112
 tests for, 113
 with gastric cancer, 112
 Open treatment of wounds, 252
 Operating room in trenches, 249
 Operation, exploratory, in nerve injury,
 288
 for varicocele, new, 217
 Operations for painful nerve injuries, 293
 Operative methods in nerve injury, 288
 treatment of gunshot fractures, 271
 Opium, 417
 derivatives, effect of, on gastro-
 intestinal tract of man, 117
 Optochin, 421
 in pneumonia, 421
 Orthopedics, military, 268
 Ossifying myositis, 309
 Osteomalacia, 339
 Ostitis deformans, 337
 and sarcoma, 339
 fibrosa, bone cysts and, 324
 without cysts, 325
 Oxygen injections, dangers of, 277
 Oxyproteic acid test in gastric ulcer, 52

P

PANCREAS, diseases of, 132
 Pancreatic calculi, 136
 disease, amylase in, diagnostic value
 of, 135
 secretion, 132
 Pancreatitis, experimental, cause of death
 in, 135
 Paper test for free hydrochloric acid, 78
 Parathyroid gland in paralysis agitans,
 422
 Pasteurization of milk, 394
 Pelvis, giant-cell tumor of, 350
 Penis, 221
 Pepsin, 422
 nature of, 80
 Perforating ulcer of foot, 300
 Perforation of duodenal ulcer, 85
 Perinephritic abscess, 191
 Peritonitis, chronic, abdominal fremitus
 as a sign of, 83
 Phalanx, giant-cell tumor of, 351
 Phenol, 425
 poisoning, efficacy of lavage in, 425
 in treatment of wounds, 426
 Phenolphthalein, 428
 Phenoltetrachlorophthalein test for liver
 function, 128
 Phlegmons, gas, 275
 Phthalein test in orthostatic albuminuria,
 142
 Pituitary gland, 428
 in abortion, 429
 in bronchial asthma, 429
 function of anterior lobe of, 431
 in labor, 430

- Pituitary gland in menorrhagia, 430
 in metrorrhagia, 430
 in obstetric practice, 429
 as peristaltic stimulant, 429
- Pneumonia, optochin in, 421
 vaccines in, 451
- Poliomyelitis, serum treatment of, 375
- Pollen toxin in treatment of hay fever, 431
- Potassium iodide, 432
 effect of, on luetin reaction, 432
- Preoperative treatment, 232
- Prepuce, fibromyoma of, 222
- Pressure of bile during obstruction of ductus choledochus, 132
- Prostate, 199
 cysts of, 206
 syphilis of, 204
 tuberculosis of, primary, 205
- Prostatectomy, 199
- Prostatitis, metastatic, 208
- Protease intoxication in intestinal obstruction, 110
- Psychic shock, 229
- Ptyalin, function of, 19
- Puerperal fever, vaccines in, 452
- Pyelography, 184
- Pylorus, experimental partial stenosis of, and motility of empty stomach, 68
- Pyoculture, 274

Q

- QUININE, 433
 hydrochloride as a dressing for wounds, 435
 in hyperthyroidism, 436
 intravenous administration of, 434
 in malarial hemoglobinuria, 435
 as specific for gas bacillus, 276

R

- RADIUM, 436
 in cancer of pelvic organs, 437
 of uterus, 437
- Reaction of bile, 119
- Rectal feeding, 118
- Renal calculi, 179
 disease, acidosis in, 159
 functional tests, 141
 infection, lymphatic, ascending, 188
 test-meal, 143
 tuberculosis, 176, 192
 tumors, 193
- Residual nitrogen in liver disease, 129
- Respiration, artificial, 378
- Rhabdomatous sarcoma, 208
- Rheumatic fever, salicylates in, 438
- Rupture of kidney, 189
 of muscle, 306

S

- SALICYLATES, 438
 in childhood, 439

- Salicylates in rheumatic fever, 438
 in scarlet fever, 441
- Saline solution, 442
- Saliva, effect of posterior lobe of hypophysis upon secretion of, 18
 relation of, to peptic digestion, 19
 viscosity of, 17
- Salt sacks for drainage of wounds, 260
- Sarcoma of bone, 333
 and trauma, 364
 hemorrhagic cystic, 362
 ostitis deformans and, 339
 rhabdomatous, 208
- Scarlet fever, salicylates in, 441
 serum treatment of, 376
- Sciatica, saline injections in, 442
- Secretion, gastric, fraction method of examining, 74
 pancreatic, 132
- Seminal vesicles, 209
 infection of, 209
- Sensitized vaccines, 450
- Sera, antitoxic, 370
 antidiphtheric, 370
- Serum, antimeningococcic, in gonorrheal ureteropyelitis, 187
 antitetanic, 372
 blood, 384
 sickness, 377
 therapy, 278
 treatment of poliomyelitis, 375
 of scarlet fever, 376
 of trichinosis, 376
- Shock, 229
 electric, 237
 flatulence and, 239
 heart massage in, 240
 intrapericardial injections of epinephrin in, 240
 intravenous gelatin solution in, 240
 miscellaneous literature on, 239
 morphine in, 240
 nervous, importance of lumbar puncture in, 239
 operative, 231
 psychic, 229
 traumatic, 237
- Silver nitrate, 442
 in diarrhea, 442
- Skin, 297
 diseases, heliotherapy in, 406
 x-rays in, 456
 grafting, 297
 lesion, synovial, 301
 pinch grafts of, 297
 tubercle, 302
 ulcer of, tanner's, 298
- Sodium bicarbonate, 442
 in acidosis in children, 443
 in surgery, 443
- Spermatic cord, 209
- Splanchnoptosis, relations of, to gastric acidity, 58
- Stasis, intestinal, 101
 Keith's theory of, 104
- Stomach, cancer of, 40
 concrement in, 72
 diseases of, 23

- Stomach, glands of, benign proliferation of, 54
 movements of empty, in pathological states, 73
 myoma of, 72
 normal, position of, 82
 studies on, 73
 syphilis of, 68
 ulcer of, 23
- Stricture of ureter, inflammatory, 194
- Strontium salicylate, 439
- Studies on normal stomach, 73
- Sunlight in wound treatment, 254
- Surgery, accident, 244
 of extremities, 229
 military, 248
 organization in, 248
 sodium bicarbonate in, 443
- Surgical bacteriology, 272
- Suture, primary, of wounds, excision and, 261
- Synovial skin lesion, 301
- Syphilis of prostate, 204
 of stomach, 68

T

- TANNER'S ulcer of skin, 298
- Tendon-sheath tumors, 318
- Tendons, 313
 of hand, infection of, 313
 transplantation of, 314
 wounds of, 314
- Test, galactose, for liver function, 128
 phenoltetrachlorophthalein, for liver function, 128
 for urobilin in urine and feces, 128
- Test-meal, renal, 143
- Testicle, tumors of, 216
- Testicles, 209
- Tests, laboratory, for gastric ulcer, 47
 for occult blood, 113
- Tetanus, 280
 late, 281
 magnesium sulphate in, 411
- Tethelin, 444
- Thymus death, 241
 enlargement of, α -rays in, 455
- Thyroid tumors of bone, 361
- Tongue, nervous furring of, 19
- Transfusion, blood, 385, 445
- Transplantation of bone, 365
 of fibula for humerus, 368
 of tendons, 314
- Transportation of wounded, 250
- Trauma, sarcoma of bone and, 364
- Traumatic asphyxia, 238
 shock, 237
- Trench nephritis, 175
- Trenches, operating room in, 249
- Trigonitis, chronic, treatment of, 199
- Tubercle of skin, 302
- Tuberculosis of prostate, primary, 205
 pulmonary, hypophosphites in, 407
 α -rays in, 455
 renal, 176, 192
- Tumor autolysates in treatment of gastric ulcer, 52
 giant-cell, of bone, 342
 amputation in, 345
 recurrence of, 349
 spontaneous disappearance, of, 342
 of pelvis, 350
 of phalanx, 351
- Tumors of bone, metastatic, 358
 thyroid, 361
 renal, 193
 tendon-sheath, 318
 of testicle, 216
 vesical, malignant, diathermy in treatment of, 197
 mesothorium in treatment of, 197
- Typhoid fever, vaccines in, 452
 gastritis, 60

U

- ULCER, duodenal, 23, 83
 chemism of stomach with, 88
 differential diagnosis of, 84
 gastric juice in, 38
 hyperacidity and, 86
 new symptoms of, 84
 perforation of, 85
- gastric, 23
 adrenalectomy and, 40
 and cancer, 53
 and hyperacidity diet, 30
 carbohydrate factor in treatment of, 28
 cause of, 33
 experimental, 31, 39
 bacterial studies in, 38
 effect of gastric juice on, 35
 gastric juice in, 38
 gastrojejunal, 53
 perforating, of foot, 300
 tanner's, of skin, 298
- Umbilical dyspepsia, 72
- Unit plan for base hospital, 250
- Urea excretion, Ambard and Weill's coefficient of, 152
- Ureter, stricture of, inflammatory, 19
- Ureteral calculi, 179
- Ureteropyelitis, gonorrheal, treated by antimeningococcic serum, 187
- Ureters, 179
- Urethra, 221
 carcinoma of, primary, 223
 posterior, cysts of, 225
 prostatic, new growths of, in relation to tuberculosis, 226
- Urethral lesions, high-frequency current in, 224
- Urinary findings in hepatic disease, 130
- Urine color test in gastric ulcer, 52
- Urobilin, test for, in urine and feces, 128
- Urticaria, 303
- Uterus, cancer of, radium in, 437

V

VACCINATIONS, combined, 450

Vaccines, 448

in asthma, 451

autogenous, 449

commercial, 448

in gonorrhea, 451

in pneumonia, 451

in puerperal fever, 452

sensitized, 450

typhoid, 452

Varicocele, new operation for, 217

Venesection, 454

Vertigo, gastric, 71

Vesical tumors, diathermy in treatment of, 197

mesothorium in treatment of malignant, 197

Vessels, abdominal, arteriosclerosis of, 83

Visceroptosis, 58

Volkmann's contraction, 309

W

WAR neuroses, 229

Wound treatment, 247, 252

air in, 254

antiseptics in, 252

Carrel's method of, 256

continuous irrigation in, 256

Dakin's solution in, 254

irrigation in, 259

lymph lavage in, 260

open, 252

sunlight in, 254

Wounded, transportation of, 250

Wounds, excision and primary suture of, 261

foreign bodies in, 273

granulating, 262

gunshot, 250

Wounds, gunshot, drugs in treatment of, 251

general, 250

of joints, 263

bacteriological control of, 265

first treatment of, 263

hyperemia in, 265

position for ankylosed

joints after, 261

resection after, 267

of hand, 263

location of foreign body in, 261

phenol in treatment of, 428

quinine hydrochloride as a dressing for, 435

salt sacks for drainage of, 260

secondary hemorrhage in, 262

of skull in war, lumbar puncture in, 239

of tendons, 314

X

X-RAY diagnosis of gastric ulcer, 41

X-rays, 455

in enlargement of thymus, 455

in gas phlegmon, 280

in pulmonary tuberculosis, 455

in skin diseases, 456

in uterine fibroids, 456

hemorrhage, 456

value of, in diagnosing esophageal conditions, 22

in venereal buboes, 457

Y

YEAST, 457

in beriberi, 457



University of Toronto
Library

Biological
& Medical
Serials

**DO NOT
REMOVE
THE
CARD
FROM
THIS
POCKET**

Acme Library Card Pocket
Under Pat. "Ref. Index File"
Made by LIBRARY BUREAU

